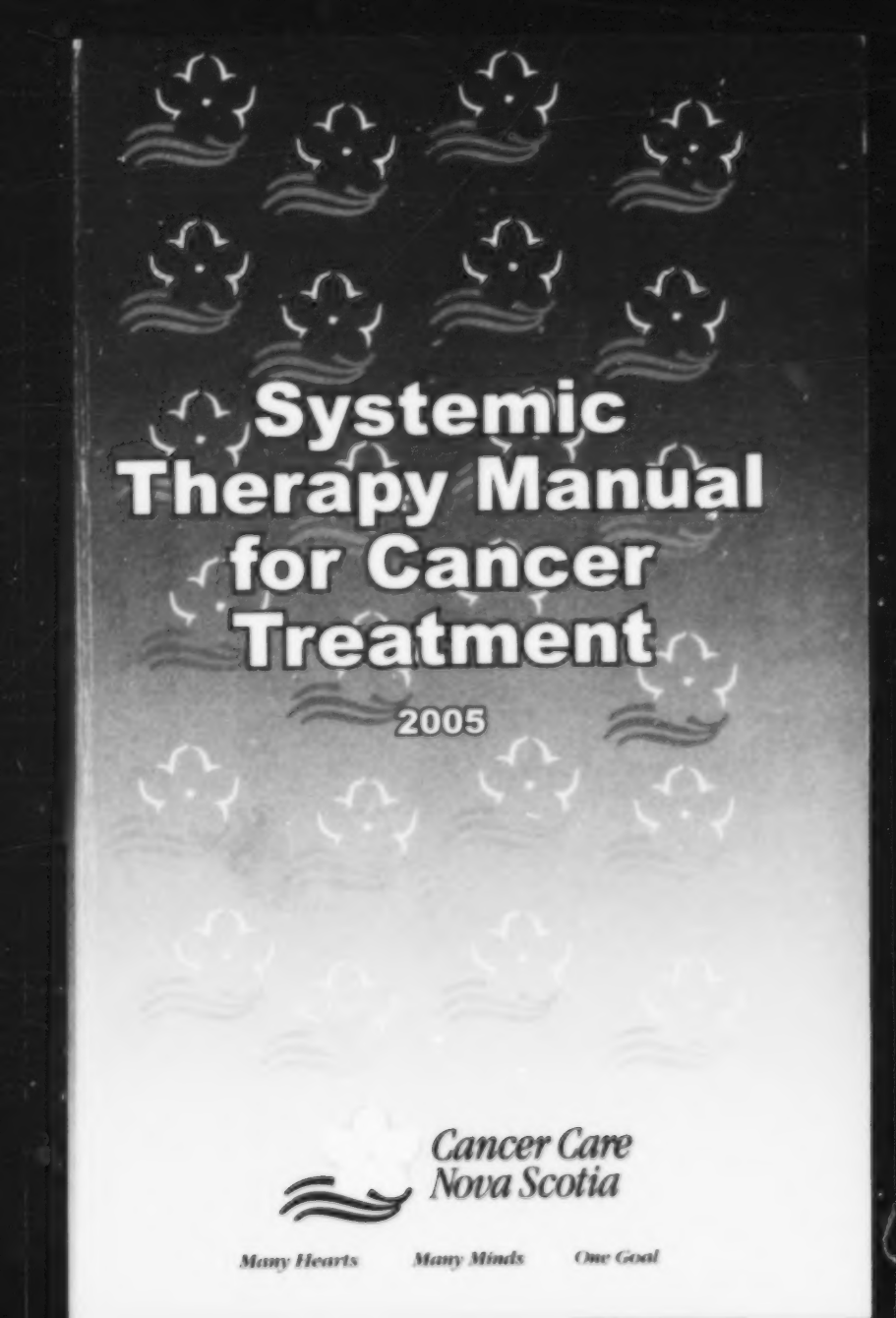




Systemic Therapy Manual for Cancer Treatment

2005



*Cancer Care
Nova Scotia*

Many Hearts

Many Minds

One Goal

**SYSTEMIC THERAPY
MANUAL FOR
CANCER TREATMENT
*POCKETBOOK VERSION***

FIRST EDITION

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Manager, Systemic Therapy Program

Published by: *Cancer Care Nova Scotia*
Dr. Andrew Padmos, Commissioner

September 2004

ACKNOWLEDGEMENTS

*This manual could not have been completed without
the help of many people.*

In particular, I wish to acknowledge:

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Cancer Care Nova Scotia, for moral and financial support;*

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CCNS, for thoughtful and detailed review and input to regimen
monographs;*

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and other Oncology Centres in Atlantic Canada for review of the
drug monographs;*

*Heidi Smeltzer, Christine Smith and Susan MacLeod of CCNS
for direction and insight in review of graphic design aspects of this
volume.*

Preface from the Editor- Full Version

The Systemic Therapy Manual for Cancer Treatment is intended to be a comprehensive and contemporary source of information for health care professionals involved with the treatment of cancer patients in Nova Scotia. The information contained within is under constant review, to be as accurate and as current as we can achieve.

Nova Scotia is a small province with both urban and rural communities. The needs of patients may vary between city and country. Patients generally do not wish to travel any further than necessary for regular treatment visits, so there is demand for treatment services in local communities, as well as tertiary sites in metropolitan areas. One goal of this Manual is to identify which treatment regimens ought to be given in tertiary sites only, in regional hospitals, and in smaller community hospitals, based upon objective criteria for safety during drug administration. This is an important component of the Levels of Care initiative, and will set reasonable expectations for patients and caregivers alike.

It is important to recognize that the actual choice of treatment regimen is meant to be an informed decision of each patient, on the advice of the physician(s) who are responsible for the patient's care. The information in this Manual is not intended to be prescriptive or restrictive, but rather to provide the necessary information to health care professionals, available when they need the information. Thus, even treatment regimens which would only be given in specialist units in the QEII Health Sciences Centre are included, to provide information to any health care professional who may be involved in patient care, at any stage of the disease continuum. If a patient returns home after a treatment, local caregivers might still need to have some appreciation of which drugs were given, when, and with what potential adverse effects.

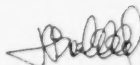
In an effort to maintain currency, we are distributing a limited number of copies of this Manual. Updates will be circulated periodically to named individuals who are responsible for copies of the Manual. For front-line users, a pocketbook version is under development for day-to-day use. If you notice any details which appear incorrect, or which may require updating, or if you have any comments on this Manual, please complete and sign the feedback form enclosed in this Manual. Another option is to visit the *Cancer Care Nova Scotia* website at www.cancercare.ns.ca, where the most current version of all materials will be posted. Feedback forms will also be available on the website.

The information contained in the Manual is within the public domain, but is not written for a lay audience. When providing written material for patients and lay public on drug therapy, we recommend the Medication Info Sheets, available for most drugs used in the systemic treatment of cancer or its symptoms. These sheets are also available for printing or downloading from the website, and are kept in stock at most hospitals in Nova Scotia.

Monograph information on individual drugs or regimens does not infer that any item is necessarily available for use at any site within the province. This is

purely information for the health care professional. Decisions on drug availability at any site is the responsibility of local decision-makers. A Nova Scotia Formulary for Cancer Agents is included with this Manual, which may assist health care districts to determine which drugs are available at local sites. Cancer Site Teams are also developing clinical guidelines for several types of cancers, which may assist in decision making.

I hope this Manual will become a valuable tool for all health care professionals who care for cancer patients in Nova Scotia!



Larry Broadfield
March 2004

Addendum to Preface- Pocketbook Version

We are pleased to follow the completion of the Systemic Therapy Manual for Cancer Treatment with this Pocketbook Version. Many of the drug monographs and regimens have been repackaged into a smaller size, for convenient use by health care professionals. We hope this will make it easier to use and that the Pocketbook Version will be a valuable tool for day to day users.

This Pocketbook Version contains information as at the date of publication. For up-to-date information on the most recent changes to this Manual, please visit our website or refer to a copy of the full version of the Manual.

If you find any material that you are uncertain about, or which may require amendment, please contact me at the general email address for Cancer Care Nova Scotia, info@ccns.nshealth.ca, or by phone at 1.866.599.2267. Your comments and feedback will be welcome and appreciated.

Larry Broadfield
March 2005

Foreword

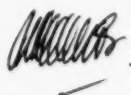
The publication of the first edition of the Systemic Therapy Manual for cancer health professionals represents a major milestone achievement for *Cancer Care Nova Scotia*, as information and ready access to comprehensive standards and regimens for systemic therapy delivery are key to ensuring a quality cancer system.

Integration of information in this manual with delivery system structures and systemic therapy policies will help ensure that cancer patients receive their treatment in the right location (as close to their home as is safely possible) by the right health professionals, who have the technical information necessary to provide treatment based on the latest evidence.

I would like to congratulate the many individuals who worked to develop this important publication, including members from *Cancer Care Nova Scotia's* Cancer Site Teams and its Systemic Therapy Program. Larry Broadfield deserves special recognition for his leadership and dedication to this project.

I hope this manual provides you with the information you need to enhance your decision making and ability to treat and care for cancer patients.

We welcome your comments by email at info@ccns.nshealth.ca, by phone at 1 866 599 2267.



Andrew Padmos, Commissioner
Cancer Care Nova Scotia

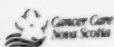


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NOTE: Drug names in italics are not in this pocketbook version- See full version for drug monograph



LEGEND FOR DRUG MONOGRAPHS

(Pharmacologic Class of Agent)

Revision Date:

COMMERCIAL PRODUCT DESCRIPTION

Brand name(s) and physical description of commercial product(s) in Canada. Also, any comments on product availability or restrictions.

MECHANISM OF ACTION

Pharmacologic mechanism by which the drug works, if known

PHARMACOKINETICS

Oral Absorption

Is the drug absorbed on oral administration?

Distribution

cross blood brain barrier?

Vd volume of distribution

PPB plasma protein bound

Metabolism

method of drug metabolism, if known

metabolite(s) active inactive

Excretion

excretion pathway(s)

urine excretion in urine

t_{1/2} serum half life

Cl serum clearance

IV COMPATIBILITY

intravenous solutions physically compatible with the drug

ROUTES

parenteral route(s) of drug administration

ADMINISTRATION

specific details for IV administration

EXTRAVASATION HAZARD

risk(s) from IV extravasation;
suggestions for management

INDICATIONS AND OTHER USES

Official reasons why this drug may be given to a patient, as approved by Health Canada and listed in an official drug monograph (see Compendium of Pharmaceuticals and Specialties for monographs)

OTHER ONCOLOGY USES

Other reasons why this drug has been used in treatment of cancer patients- these uses are NOT officially approved by Health Canada, but often proven through clinical trials.

DOSING

Common or officially approved dosing for the drug. May include different dosing for different indications
However, there may be other dosing schedules for the drug, as indicated by other regimens developed over time (warning statement below).

Other dosing may be indicated in specific regimens

SIGNIFICANT INTERACTIONS

known drugs or foods which may interact with the drug

See Appendix 3C for discussion and details on hepatic enzyme subtypes and how these may predict for potential drug-drug interactions

CONTRAINDICATIONS

- known reasons why this drug should NOT be given to a patient

ANTIEMETIC RISK

RISK LEVEL (Percentage of patients with emesis)

- Usual drug recommendations pre-chemotherapy and post-chemotherapy from "Guidelines For The Management Of Nausea & Vomiting In Cancer Patients" (CCNS Guidelines)

See Nausea & Vomiting Guidelines for more detail

Continued Next Page...

LEGEND FOR DRUG MONOGRAPHS

SIDE EFFECTS

* may be life-threatening

side effects in **bold**, *italic* type are common

IMMEDIATE ONSET

side effects which can occur within hours to days of administration

EARLY ONSET

side effects which can occur within days to weeks of administration

DELAYED/LATE ONSET

side effects which can occur within weeks to years of administration

CLINICAL MONITORING

RECOMMENDED CRITERIA

These monitoring criteria and toxicity ratings are **RECOMMENDED** for routine practice

→ Toxicity ratings and relevant lab results are to be documented

SUGGESTED CRITERIA

These monitoring criteria and toxicity ratings are **SUGGESTED** for consideration by the prescriber and

primary caregivers; these are not required

PHARMACEUTICAL CONSIDERATIONS

Dosage forms, contents, storage and handling criteria. Preparation criteria.

Selected stability and compatibility information. Other information about the pharmaceutical preparation(s), as appropriate

DOSE ADJUSTMENT CRITERIA

Criteria for dose adjustment, based upon organ dysfunction or other factors which could influence a dose change.

Adjustments for myelosuppression are listed with individual regimens.

Suggested adjustments in italics (little or no evidence to support specific adjustments)

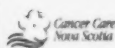
Recommended adjustments in bold print (good evidence or specific citation in approved drug monograph to support adjustment criteria)

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
*Basic-Intermediate-Advanced-
Specialty Levels- Drug acuity levels
for provincial Managed Systemic
Therapy Program*

CDHA Status *Formulary
Inclusion noted*

Pharmacare Status *Formulary
Inclusion noted; Specific restrictions
may apply; where guidelines or
specific approval exist, these are
noted*

**ANASTROZOLE**

(Antineoplastic Agent; Aromatase Inhibitor)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Arimidex®

White tablets with 1mg Anastrozole

MECHANISM OF ACTION

Selective, nonsteroidal aromatase inhibitor, with no detectable effect on synthesis of adrenal corticosteroids or aldosterone. It inhibits the activity of aromatase enzyme responsible for the conversion of androstenedione to estrone, and testosterone to estradiol. Causes an 85% reduction in estrone sulfate levels.

PHARMACOKINETICSOral Absorption

well absorbed (80%), may be absorbed in the presence of food

Distribution

crosses the placenta; Excretion in breast milk unknown

Vd no information PPB 40%

Metabolism

hepatic- N-deallylation, hydroxylation, glucuronidation

metabolite(s) active- no information
inactive- triazole (1st metabolite)

Excretion

biliary 85%, renal 11% (~10% unchanged, 60% as metabolites), urine yes

ROUTES

oral

DOSING

- **1 mg PO once daily.**
 - Administer with food or on empty stomach.
- Pediatric:* Limited data on the use of this
Other dosing may be indicated in specific regimens

INDICATIONS AND OTHER USES

- Breast cancer

CONTRAINDICATIONS

- pregnant or lactating women
- patients with thromboembolic conditions, pulmonary emboli, DVT, thromboembolic stroke

SIDE EFFECTS

- may be life-threatening side effects in ***bold, italic*** type are common

EARLY ONSET (days to weeks)

chest pain
dyspnea
peripheral edema

CLINICAL MONITORINGRECOMMENDED CRITERIA

NO RECOMMENDED TOXICITY RATINGS

SUGGESTED CRITERIA

NO ADDITIONAL TOXICITY RATINGS

SIGNIFICANT INTERACTIONS

Tamoxifen
Cytochrome P-450 1A2, 2C8/9, 3A4 substrate

PHARMACEUTICAL CONSIDERATIONS

Tablet: 1 mg; inactive ingredient includes lactose.

Store at room temperature.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level: Take home
prescription on preprinted Physician
Standing Order

CDHA Formulary Status Formulary
Pharmacare Status Formulary

NOTE: It is recommended to order this medication on preprinted Physician Standing Order form, for patient safety

APREPITANT

(Antiemetic, Neurokinin-1 [NK-1]-Antagonist)

Revision Date Oct 03

DRUG

COMMERCIAL PRODUCT DESCRIPTION

U.S. Brand Name: Emend®

White capsules with 80mg, white/pink capsules with 125mg

Not Available in Canada- May be available on a case-by-case basis through Special Access Program, Health Canada (call 613-941-2108 /e-mail EDR_Drugs-

MECHANISM OF ACTION

Selective neurokinin-1 receptor (NK-1) antagonist, acting at central NK-1 receptors.

PHARMACOKINETICS

Oral Absorption

well absorbed, bioavailability 60% to 65%
C_{max} at about 4 hours, not affected by food

Distribution

cross blood brain barrier? Yes
V_d 70 L PPB >95%

Metabolism

Extensively metabolized by CYP3A4
(minor routes by CYP1A2 & CYP2C19);
oxidation at morpholine ring & side
chains. Some metabolites with weak
activity

Elimination

Eliminated primarily by metabolism, not
renal excretion. Urine 57%, mostly as
metabolites, ~45% in the feces.

Cl 62-90 mL/min t_{1/2} Elimination 9-13

ROUTES

oral

ADMINISTRATION

- Take 125mg by mouth before chemotherapy (on Day 1) and 80mg by mouth on Days 2 & 3
- May be given with a serotonin receptor antagonist and steroid on Day 1 and with a steroid on Days 2 & 3 (steroid alone on Day 4)
- Reduce dexamethasone pre-chemotherapy to 12mg, and 8 mg on Days 2-4

INDICATIONS AND OTHER USES

Prevention of acute and delayed nausea & vomiting from highly emetogenic chemotherapy

SIDE EFFECTS

* may be life-threatening; side effects in **bold**, *italic* type are common

EARLY ONSET (days to weeks)

constipation, diarrhea
fatigue

CLINICAL MONITORING

RECOMMENDED CRITERIA

NO RECOMMENDED TOXICITY
RATINGS

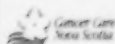
SUGGESTED CRITERIA

NO ADDITIONAL TOXICITY RATINGS

CONTRAINDICATIONS

- sensitivity to any component of the product
- moderate cytochrome P-450 3A4 enzyme inhibitor, should not be used concurrently with any CYP3A4 substrate (eg, pimozone, terfenadine, astemizole, or cisapride) which could be elevated in the plasma and which could thereby cause potentially life-threatening reactions.

Continued Next Page...



APREPITANT

SIGNIFICANT INTERACTIONS

Aprepitant is a moderate cytochrome P450 3A4 enzyme inhibitor. should be used with caution when given concurrently with any CYP3A4 substrates, such as:

- Chemotherapy agents (e.g. docetaxel, paclitaxel, etoposide, irinotecan, ifosfamide, imatinib, vinorelbine, vinblastine, vincristine) (e.g. pimozide, terfenadine, astemizole, or cisapride)
- warfarin, tolbutamide
- oral contraceptives
- corticosteroids (reduce dose for equivalent effect)

Aprepitant is also a CYP3A4 enzyme substrate. should be used with caution when given concurrently with any strong CYP3A4 inducer (e.g. rifampin, carbamazepine, phenytoin), or strong CYP3A4 inhibitor (e.g. ketoconazole, itraconazole, nefazodone, troleanandomycin, clarithromycin, nifedipine, nelfinavir, diltiazem)

ADMINISTRATIVE INFORMATION

When available in Canada

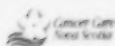
CCNS Provincial Formulary Status-
Basic Level and Take Home
Prescription

CDHA Status Non-Formulary

Pharmacare Status Non-Formulary

EMERGING INFORMATION

This drug is under investigation and has not been widely used in oncology practice. As new information is discovered, portions of this monograph may become outdated. Refer to primary literature and revisions to official product monograph to ensure that information on this drug is current.

**ASPARAGINASE; ASPARAGINASE ERWINIA**

(Antineoplastic Agent)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Kidrolase® Vials of 10,000IU Asparaginase for reconstitution with 4mL Sterile Water for Injection- Keep refrigerated

- Kidrolase removed from Canadian Market. Asparaginase Erwinia never released
- Available on a case-by-case basis through Special Access Program. Health Canada (call 613-941-2108 /e-mail EDR_Drugs-BPA@hc-sc.gc.ca)

MECHANISM OF ACTION

Contains 1-asparaginase amidohydrolase type EC-2, which inhibits protein synthesis by hydrolyzing asparagine to aspartic acid and ammonia. Leukemic cells, especially lymphoblasts, require exogenous asparagine; normal cells can synthesize asparagine. Asparaginase is cycle specific for the G1 phase of the cell cycle. Asparaginase extracted from *E. coli* or *erwinia* sp.; *erwinia* source asparaginase limited to patient with allergy to *E. coli* proteins.

PHARMACOKINETICSOral Absorption

no

Distribution

most of an IV dose remains in the plasma. IM injection yields a much larger volume of distribution (plasma levels about 50% lower than with IV). Excretion in breast-milk unknown.

cross blood brain barrier? minimal

Vd 245 ± 28 mL/kg (IM); 63 ± 7 mL/kg

PPB low

Metabolism

systemic; major route of elimination; possible mechanisms include proteolysis of the enzyme and/or removal by an organ other than the kidney (eg. reticuloendothelial system)

Metabolite(s) active- none known
inactive- yes

Excretion

Reticuloendothelial system; minimal excretion into urine and bile

Urine trace

t½ 27-32 hours (*E. coli*, IM); 16 hours (*Erwinia*, IM); 7-8 hours (IV)

Cl no information

ROUTES

intramuscular (preferred, maximum 2 mL per site)

intermittent IV (in 50-150 mL D5W over 15-30 minutes)

subcutaneous

ADMINISTRATION

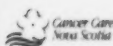
- Given as an IM injection (preferred route) (maximum concentration of 2000 IU/mL)
- Mix in 100mL minibag (5% Dextrose, Normal Saline) or slow push through sidearm of free flowing IV (5% Dextrose, Normal Saline). Infuse over at least 30 minutes
- Hypersensitivity reactions (frequent). May occur with any dose including the first, but appear to be more common with multiple prior doses. Reactions typically present within ½-2 hours following administration. Clinical manifestations of hypersensitivity (Type I - immediate) may include pruritus, dyspnea, agitation, urticaria, swelling at the injection site, angioedema, rash, abdominal pain, laryngospasm, nasal stuffiness, bronchospasm, hypotension and may progress to life threatening anaphylaxis. Respiratory support equipment, epinephrine, antihistamines, corticosteroids and physician support must be readily available.

IV COMPATIBILITY

normal saline, dextrose 5% (discard if cloudy), sterile water for injection

EXTRAVASATION HAZARD

None



ASPARAGINASE; ASPARAGINASE ERWINIA

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

- * **anaphylaxis (6-43% allergic reactions, 1% mortality)**
- nausea and vomiting
- increased uric acid levels (hyperuricemia)**

DELAYED/LATE ONSET (weeks

to years)

- * inflammation of pancreas (pancreatitis)
- * liver problems (hepatic necrosis)
- * blood clotting problems (1-2%, coagulopathy)
- central nervous system problems (21-60%, depression, confusion, personality changes)**

EARLY ONSET (days to weeks)

- * liver problems (elevated liver function tests, parenchymal necrosis)
- * blood clotting problems (1-2%, coagulopathy)
- * low WBC, RBC, platelets (myelosuppression)
- central nervous system problems (21-60%, depression, confusion, personality changes)**
- * kidney problems (toxic nephropathy)
- * high blood glucose levels (hyperglycemia)
- * inflammation of pancreas (pancreatitis)

DOSING

IM and IV doses are equivalent.

Induction:

- daily (usual method and less likely to cause adverse effects)
- 6,000-10,000 IU/m²/day x 6-14 days
- 200-1000 IU/kg/day IM/IV x 28 days; may continue additional 14 days if remission not achieved
- tiw (= 3 times per week): 400 IU/kg - 400 IU/kg - 600 IU/kg MWF x 28 days; may continue additional 14 days if remission not achieved

Reinduction:

- q1w: 3,000 IU/m²/day IV x 5 days

Pediatric:

Intramuscular: tiw (= 3 times per week):

6,000 IU/m² x 9 doses (some protocols use 200 IU/kg for children <3 years of age)

q7-10d: 10,000 IU/m²/day IV

q1w: 25,000 IU/m²/day IM

Other dosing may be indicated in specific regimens

INDICATIONS AND OTHER USES

- Acute lymphocytic leukemia
- Acute myeloblastic leukemia
- Acute myelomonocytic leukemia
- Chronic lymphocytic leukemia
- Hodgkin's disease
- Melanosarcoma

OTHER ONCOLOGY USES (Not Approved)

Non-Hodgkin's lymphoma

CONTRAINDICATIONS

- known hypersensitivity to asparaginase
- pregnancy and breast feeding
- history of pancreatitis

SIGNIFICANT INTERACTIONS

cytarabine, etoposide, methotrexate, prednisone, vincristine (give asparaginase last on treatment day)

serum thyroxine-binding globulin, cyclophosphamide, mercaptopurine, prednisone

ANTIEMETIC RISK

LOW RISK (Less than 10% of patients)

- No routine antiemetic pre-chemotherapy or post-chemotherapy

See Nausea & Vomiting Guidelines

DOSE ADJUSTMENT CRITERIA

Hepatic failure (*Suggested action*)

Treatment should be discontinued if hepatic failure develops.

Continued Next Page...

ASPARAGINASE; ASPARAGINASE ERWINIA

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Observation for hypersensitivity reaction during and for 30 minutes after injection (emergency treatment readily available)
- Intradermal skin test prior to first dose and other doses if more than 1 week between doses.

SUGGESTED CRITERIA

- Baseline & periodic liver function tests [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- Baseline & periodic serum amylase levels & serum glucose levels

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Intermediate Level

CDHA Status Formulary

Pharmacare Status Formulary (red)

PHARMACEUTICAL CONSIDERATIONS

Injection

10,000 IU vial. Storage in the refrigerator is recommended. One reference [Vogenberg] states that intact asparaginase Kidrolase vials are stable for at least 48 hours at room temperature while another [King] states that they are stable for 1 year at room temperature. Intact *asparaginase Erwinia* vials should be refrigerated but are stable for 6 weeks at room temperature.

Reconstitute powder with 4 mL SWI or NS to a final concentration of 2,500 IU/mL. For IM injection, Trissel recommends reconstitution with 2 mL NS to give a final concentration of 5,000 IU/mL. For IM injections of high dose therapy (10,000 IU), the 10,000 IU vial can be reconstituted with 0.5 mL of NS to give a final concentration of 20,000 IU/mL. If >2mL solution is need, prepare in 2 syringes for injection into 2 different sites. To avoid foaming, rotate gently; do not shake.

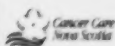
Reconstituted solution for injection

Kidrolase® solution maintains potency for 14 days when refrigerated and for 7 days at room temperature; storage in the refrigerator is recommended. Cloudy solutions should be discarded. Small numbers of gelatinous fibres may develop in Kidrolase solution on standing. Filtering through a 5 micron filter will remove the fibres with no loss of potency, but filtration through a 0.2 micron filter may result in some loss of potency. *Asparaginase Erwinia* solution is stable for up to 20 days when refrigerated or stored at room temperature. Cloudy solutions should be discarded. However, to minimize protein denaturation which may occur from contact with the vial stopper, withdraw *asparaginase Erwinia* solution from the vial within 15 minutes of reconstitution.

Diluted solution for infusion

Kidrolase is stable in D5W or NS for up to 8 hours, provided that the solution remains clear. Suitable volumes of D5W or NS for dilution are 50-150 mL. Dilutions of *asparaginase Erwinia* 35 IU/mL in D5W or NS are stable for 4 days when refrigerated or stored at room temperature. Loss of activity and denaturation may occur outside pH range of 6-7.5.

It is recommended that *asparaginase* not be mixed with other drugs.



BCG (Bacillus Calmette-Guérin)

(Antineoplastic Agent)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Names: ImmuCyst® Vials with 81 mg BCG for reconstitution
 OncoTICE® Vials with 1 to 8 x 10⁸ colony forming units of Tice-strain BCG
 PACIS® Ampules of 120 mg (2 to 10 x 10⁸ colony forming units) of BCG
 Keep refrigerated, protect from light (Vials of PACIS should be stored at -30°C)

MECHANISM OF ACTION

Mechanism of action is not clear. A proposed mechanism is that the antitumor effect is related to release of tumour necrosis factor from activated macrophages. Local chronic inflammation follows, leading to destruction of superficial tumour cells.

PHARMACOKINETICS

Pharmakodynamic/kinetic data have not been reported

IV COMPATIBILITY

normal saline (preservative-free)

DOSING

Intravesical

- OncoTICE™ 1 ampul diluted to 30-50 mL Instil weekly for 6 weeks, then on weeks 8 & 12, then monthly for months 4 to 12 (1 to 8 x 10⁸ CFU/ampul - Organon brand)
- ImmuCyst™ 1 ampul diluted to 30-50 mL Instil weekly for 6 weeks, then at 3, 6, 12, 18 & 24 months (81 mg/ampul - Connaught brand)
- PACIS™ 1 ampul or vial diluted to 30-50 mL Instil weekly for 6 weeks, then at 3, 6, 12, 18, & 24 months (120 mg/ampul or vial, BioChem Vaccines)
- Severe cystitis may require a 50% dose reduction

If partial response, consider further 6 week course.

Further BCG for persistent disease after 2 courses or maintenance BCG are not recommended.

Intralesional

- q1w: 0.005 mg x 4 weeks, then q2-4 weeks for 6-12 months; escalate depending on reactivity

Scarification

- up to 40 mg

Pediatric: No pediatric indications

Other dosing may be indicated in specific regimens

ROUTES

intravesical (in 50 mL unpreserved NS, 2 hour retention)
 intralesional (rarely) by physician
 scarification (rarely) by physician

ADMINISTRATION

- Instillation into the bladder (through an indwelling catheter); held in the bladder for about 30 minutes, with frequent body positioning (to coat inner surface of bladder) (*administering nurse should be certified to administer indwelling bladder instillations with chemotherapy and biologic agents*)

INDICATIONS AND OTHER USES

- Bladder cancer

OTHER ONCOLOGY USES

Malignant melanoma

CONTRAINDICATIONS

- known hypersensitivity to BCG
- pregnancy or breast feeding
- low WBC, RBC, platelets (myelosuppression)
- significant positive tuberculin skin test
- recent smallpox immunization
- burn patients
- systemic corticosteroids in the previous 6 months
- tuberculin positive patients
- AIDS patients

Continued Next Page...

BCG (Bacillus Calmette-Guérin)

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

* anaphylaxis

flu-like symptoms (fever, chills, malaise, vomiting, arthralgia, myalgia, headache)

bladder problems (cystitis, frequency, pain on urination, blood in urine, in bladder cancer)

itching (urticaria)

EARLY ONSET (days to weeks)

liver problems (elevated liver function tests)

injection site reactions

lymph node problems

(lymphadenopathy)

* disseminated BCG infection

DELAYED/LATE ONSET (weeks to years)

skin problems at injection site (granulomas)

liver problems (hepatitis, tuberculoid granulomas)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Watch for signs of **urinary infection**, especially with prolonged cystitis, hematuria, signs of systemic tuberculosis infections

SUGGESTED CRITERIA

NO ADDITIONAL TOXICITY RATINGS

SIGNIFICANT INTERACTIONS

antitubercular drugs,
immunosuppressive drugs (eg,
dexamethasone, prednisone), TB skin
test

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Basic Level: Bladder Instillation only
Community Level: Take home
prescription for administration in
physician's office

CDHA Status

Formulary

Pharmacare Status

Formulary (red)

PHARMACEUTICAL CONSIDERATIONS

Handling precautions

BCG preparations contain viable attenuated mycobacteria and should be handled as infectious material. BCG should not be handled by persons with a known immunologic deficiency. Persons handling the product should be masked and gloved. Inadvertent injection can result in a local reaction; inadvertent contact with the eye may result in severe local tissue damage and possible loss of vision. All disposable equipment and materials used for preparation and administration should be handled as biohazardous waste. Disinfectant solutions should be used to decontaminate vial stoppers before and after needle punctures. Where available, closed systems should be used.

BCG (Bacillus Calmette-Guérin)**PHARMACEUTICAL CONSIDERATIONS (continued)**Injection

BCG vaccine (freeze-dried): 1.5 mg vial (Connaught) plus diluent (buffered saline); 0.75 mg ampul (IAF BioVac) plus diluent.

ImmuCyst (Aventis Pasteur): 1) Package containing 3 vials of freeze-dried BCG, each containing 27 mg dry weight BCG, equivalent to 40 mg moist weight; package also contains 3 vials of preservative-free diluent (0.85% sodium chloride, 0.025% Tween 80, 0.06% w/v sodium di-hydrogen phosphate and 0.25% disodium hydrogen phosphate); a 50 mL vial of phosphate-buffered saline is also available for dilution prior to bladder instillation.

2) Package containing 1 vial of 81mg freeze-dried BCG (equivalent to $10.5 \pm 8.7 \times 10^8$ CFU attenuated BCG, *M. bovis*), and 1 vial with 3mL diluent solution (same preparations as above)

Reconstitute with diluent solution (3 x 1mL for 27mg vials or 3mL for 81mg vial). Shake gently to suspend contents; avoid foaming of suspension. Withdraw into 5mL syringe (3 x 1mL from 27mg vials or 3mL from 81mg vial). Transfer suspension to a larger syringe and dilute with 50mL sterile normal saline to a total volume of 53mL. *OncoTICE (Organon Teknika)*: Package with one 2mL vial containing 1 to 8×10^8 CFU Tice strain BCG as a freeze dried cake. Store in refrigerator at 2-8°C; protect from light.

Reconstitute with 1mL preservative-free normal saline; let stand for a few minutes, then gently swirl until homogenous suspension. Do not shake or agitate vial. Suspension may be stored in refrigerator at 2-8°C for up to 2 hours.

Transfer 1mL suspension to a 50mL syringe. Rinse vial with 1mL saline, and transfer this to the same 50mL syringe. Dilute suspension in syringe with normal saline to a total volume of 50mL. Do not filter concentrated or diluted suspension.

PACIS (Shire Biologics): Package with one vial or ampoule containing 120mg BCG lyophilized powder (equivalent to 2×10^8 CFU attenuated BCG, *M. bovis* substrain Montreal). Store at -30°C if possible. When product is transferred to the refrigerator at 2-8°C, the expiry date will be 6 months from the transfer date. Protect from sunlight. Powder may be kept at room temperature for up to 6 hours.

Reconstitute with 1mL sterile water for injection. Gently transfer solution into vial or ampoule; let stand for a few minutes, then withdraw contents into syringe, transfer between syringe and vial/ampoule 2 or 3 times to mix suspension. Dilute suspension in syringe with normal saline to a total volume of 50mL. Do not filter concentrated or diluted suspension.

Diluted suspension for bladder instillation

Diluted suspension should be used immediately. If there is a delay, the diluted suspension may be stored up to 2 hours before use. If flocculation or clumping is observed in any suspension, the product may be gently shaken; if the product does not re-suspend, this dose should not be used.

It is recommended that BCG not be mixed with other drugs.

Safe waste disposal

The manufacturer recommends that urine voided for 6 hours after instillation be disinfected with an equal volume of household bleach and allowed to stand for 15 minutes before flushing. This precaution is intended to protect the person flushing the toilet from splash-back of viable BCG (eg, into the eyes). No environmental impact assessment was performed.

BICALUTAMIDE

(Antiandrogen; Antineoplastic Agent)

Revision Date: Feb 03

DRUG

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Casodex®

White tablets with 50mg Bicalutamide

MECHANISM OF ACTION

Antiandrogen that inhibits androgen uptake and/or nuclear binding of androgen in target tissue.

PHARMACOKINETICS

Oral Absorption

Extensive

Distribution

widely distributed; PPB 96%

Metabolism

Hepatic, extensive; metabolism is stereospecific (active R-enantiomer is oxidized to an inactive metabolite, which undergoes glucuronidation)
metabolite(s) active- no information
inactive- yes

Excretion

renal (34%) and fecal (43%), as glucuronide derivatives urine
yes

t½ R-enantiomer: 5.8 to 7 days

Cl no information

ROUTES

oral

INDICATIONS AND OTHER USES

- Prostate cancer

CONTRAINDICATIONS

- women- especially women who are or may become pregnant

DOSING

Oral:

- **50 mg** (range 50-150 mg) **PO once daily**.

Administer with food or on an empty stomach.

Other dosing may be indicated in specific regimens

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

nausea
hot flushes
drowsiness

Therapy with a GnRH analog can inhibit initial androgenic stimulation and potential exacerbation of symptoms (e.g. bone pain, urinary obstruction, liver pain, impending spinal cord compression) during the first months

EARLY ONSET (days to weeks)

diarrhea, constipation
infection
weakness
hair loss

SIGNIFICANT INTERACTIONS

GnRH analog therapy
warfarin

CLINICAL MONITORING

SUGGESTED CRITERIA

- Periodic **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- Diabetic patients: periodic **serum glucose levels**
- Prostate specific antigen (PSA) levels at regular intervals; tumour measurements

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level Take Home
Prescription (NB. Use of preprinted
Physician Standing Order is
recommended)

CDHA Status Non-Formulary
Pharmacare Status Formulary



BLEOMYCIN

(Antineoplastic Agent, Antibiotic)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Bleinoxane®

Vials with 15mg (or 15 U) Bleomycin

Generic products available

Keep refrigerated, protect from light during storage

MECHANISM OF ACTION

Inhibits the incorporation of thymidine into DNA, inhibiting DNA synthesis; binds to DNA leading to single- and double-strand breaks; specific for G2 and M phase of the cell cycle.

PHARMACOKINETICS

Oral Absorption

no

Distribution

high concentrations in skin, lung, kidney, peritoneum and lymphatics, low concentration in testes and GI tract, crosses placenta,

cross blood brain barrier? no

Vd 0.27 L/kg, 10 L/m²

PPB <10%

Metabolism

inactivated by enzymes in many tissues, including liver

metabolite(s) inactive- yes
active- bleomycin-iron complex

Excretion

excreted by kidneys

urine 50-70% within 24 hrs, 20-40% as active drug

t_{1/2} dependent upon renal function:
normal: t_{1/2} α: 1.3 hours t_{1/2} β: 9 hours

Cl 1.1 mL/min/kg, 51.8 mL/min/m²,
70.5 mL/min/m² children <3 yrs.

IV COMPATIBILITY

normal saline, dextrose 5%

Bleomycin admixtures become less stable over time in dextrose solutions, therefore NS is used as the standard diluent.

ROUTES

- subcutaneous (SC infusion = IV infusion)
- intramuscular (no advantages over IV)
- direct IV (preferred route, ≤3 U/mL over 10 minutes)
- intermittent IV (in 50-100 mL over at least 10 minutes)
- continuous IV (in 500-1000 mL per day for 3-5 days)
- intrapleural (in 100 mL NS)
- intra-arterial (well diluted over 12-24 hours)
- intravesical (in 30-60 mL SWI, 2 hour retention)

DOSING

NOTE: 1 mg of bleomycin is equal to 1 unit.

Intravenous:

- biw-q4w: 10-20 U/m² (or IM/SC) (biw = twice a week)
- daily: 5-15 U/m² by continuous IV x 4-7 days
- q1w: 5U (or IM/SC)

Intrapleural:

- 15-240 U

Intra-arterial:

- ≤60U/day

Intraperitoneal:

- 60-150 U

Intravesical:

- 30-120 U

Other dosing may be indicated in specific regimens

EXTRAVASATION HAZARD

None

ANTIEMETIC RISK

LOW RISK (Less than 10% of patients)

- No routine antiemetic pre-chemotherapy or post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

SIGNIFICANT INTERACTIONS

amifostine, amphotericin, digoxin, oxygen/nitrous oxide, phenytoin

Continued Next Page...

BLEOMYCIN

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)

- * anaphylaxis (1-8%, pretreatment recommended-Symptoms: hypotension, fever, chills, mental confusion and wheezing)
- * **allergic** (fever, chills, pretreatment recommended)
nausea and vomiting (uncommon, usually mild)
injection site problems (phlebitis)
- * hyperpyrexia episode (excessive sweating, dehydration and hypotension)
skin problems (radiation recall reaction, rare)

EARLY ONSET (days to weeks)

- skin problems** (rash, reversible hyperpigmentation, nail changes)
mouth sores (stomatitis)
hair loss (partial alopecia)
blood problems (rare, disseminated intravascular coagulation)
vasoconstriction of extremities (Raynaud's syndrome, rare)

DELAYED/LATE ONSET (weeks to years)

- * lung problems (10% interstitial pneumonitis, 1% chronic fibrosis)
skin problems (reversible hyperpigmentation)

ADMINISTRATION

- Full dose may be mixed in 50mL minibag (Normal Saline or 5% Dextrose); Infuse over 15 minutes
- May be given by direct IV push over 5-10 minutes, followed by a Saline flush, if no IV line has been set up (*administering nurse should be certified to administer IV push chemotherapy agents*)
- May give Acetaminophen 325mg ii tabs as premedication for Bleomycin
- If the patient is known to have hypersensitivity to other drugs, the first dose may be preceded by 1U test dose mixed in 50mL Normal Saline, infused over 15 minutes. The patient is monitored every 30 minutes for 2 hours for hypersensitivity, then a premedication dose of Hydrocortisone 100mg may be given IV, followed by the balance of the Bleomycin dose given in 50mL Normal Saline over 15 minutes. Emergency drugs and resuscitation equipment must be available.
- May administer dose as a continuous infusion in 1000 mL NS and infuse over 24 hours.

Intrapleural: Administer dose in 50-100 mL NS by rapid push via thoracostomy.

DOSING

Maximum lifetime dose:

- 400 U (Count intraperitoneal and intrapleural doses as half.) When used in combination with other antineoplastic agents, pulmonary toxicities may occur at lower doses.

Pediatric:

Intravenous:

- q1w: 30 U/m² q2w: 10 U/m²
- q3-4w: 30 U/m²
- q9w: 15 U/m²/day x 3 days

Maximum lifetime dose: 250 U/m²

DOSE ADJUSTMENT CRITERIA

Renal failure (*Recommended action*)

REDUCE to 75% dose if CrCl = 12-48mL/min

REDUCE to 50% dose if CrCl < 12mL/min

ADMINISTRATIVE INFORMATION

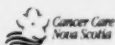
CCNS Provincial Formulary Status-
Basic Level

CDHA Status Formulary

Pharmacare Status Formulary (red)

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BLEOMYCIN



INDICATIONS AND OTHER USES

- Cervix, squamous cell cancer
- Ovarian germ cell tumors
- Head and neck cancer
- Hodgkin's disease
- Non-Hodgkin's lymphoma
- Penis, squamous cell cancer
- Skin, squamous cell cancer
- Testicular cancer
- Vulva, squamous cell cancer
- Malignant pleural effusion
- Renal cell cancer
- Soft tissue sarcomas

OTHER ONCOLOGY USES

Germ cell tumours of childhood

Kaposi's sarcoma

Leukoplakia

Osteogenic sarcoma

Prevention and management of malignant pleural effusion when administered intrapleurally

CONTRAINDICATIONS

- known hypersensitivity to bleomycin
- pregnancy and breast feeding
- severe pulmonary disease

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Clinical pulmonary exam** at each visit, including auscultation, pulmonary toxicity ratings (Cough, SOB)
- **Baseline renal function tests** (if failure suspected) [serum creatinine, electrolytes & BUN]

Cough

0. None

1. Mild

2. Moderate

3. Severe

Short Of Breath

0. No change

1. Mild SOB

2. Dyspnea on exertion

3. Dyspnea at normal level of activity

4. Dyspnea at rest

Rated At Each

Clinic Visit, If

Bleomycin

Dosage Needs

Adjustment

SUGGESTED CRITERIA

- **Periodic liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]
- **Routine pulmonary tests** if patient has pre-existing pulmonary dysfunction, or has had prior pulmonary radiation, if age >70, or if total cumulative Bleomycin dose >400

Pneumonitis

0. Normal

1. X-ray changes

2. Steroids required

3. Oxygen required

4. Assisted ventilation required

Rated When High Risk, High

Cumulative Bleomycin Dose or

Patient Symptomatic

Continued Next Page...

BLEOMYCIN

PHARMACEUTICAL CONSIDERATIONS

Injection

15 unit vial (1 unit bleomycin has equivalent activity to 1 mg bleomycin A2 reference standard). Store in refrigerator. Stable at room temperature for at least 28 days. Reconstitute powder with 5-20 mL SWI, NS, D5W or bacteriostatic water for injection. A smaller volume of diluent (eg, 1-5 mL) may be used for IM or SC administration.

Reconstituted solution for injection

Potency retained for at least 48 hours when refrigerated. Trissel reports that bleomycin reconstituted with NS is stable for 2 weeks at room temperature and 4 weeks when refrigerated, but recommends that preservative-free solutions should be used within 24 hours of reconstitution because of the risk of microbial contamination.

QEll policy states that LVP doses in 1000 mL NS are stable for 30 hours at room temperature (24 hours plus 6 hours for preparation and transportation).

Stability in syringes

A solution of 0.6 U/mL NS is reported to lose only 6% in 28 days when stored in polypropylene syringes at room temperature in the dark.

Diluted solution for infusion

The manufacturer reports stability for 8 hours at room temperature in D5W, D10W, 10% invert sugar in NS, and 20% mannitol (discard if a precipitate forms). Trissel reports little or no loss in NS but up to 16% loss in D5W when both solutions were stored for 24 hours at 23°C in either glass or PVC containers.

No significant reduction in potency was seen when 0.3 U/mL solutions in D5W or NS were filtered through 0.22 micron cellulose ester membrane (Ivex-2, Millex OR) or Teflon (Millex FG) filters.

Compatible with ondansetron. It is recommended that bleomycin not be mixed with other drugs.

BORTEZOMIB

Revision Date: Nov 04

(Antineoplastic Agent; Proteasome Inhibitor)

COMMERCIAL PRODUCT DESCRIPTION

U.S. Brand Name: Velcade™ Vials for injection with 3.5 mg Bortezomib
 Not Available in Canada- May be available on a case-by-case basis through
 Special Access Program

MECHANISM OF ACTION

Bortezomib is a reversible inhibitor of the 26S proteasome protein complex, which degrades ubiquitinated proteins. Ubiquitin-proteasome plays an essential role in the regulation of specific protein concentrations, and maintenance of cellular homeostasis. Inhibition of 26S proteasome prevents targeted proteolysis and affects multiple intracellular signalling cascades resulting in apoptosis of tumour cells.

PHARMACOKINETICSAbsorption

No information

Distribution

83% bound to plasma proteins

Metabolism

Oxidative metabolism by CYP 450 enzymes 3A4, 2D6, 2C19, 2C9 & 1A2

Major metabolic pathway by deboronation and subsequent hydroxylation

Excretion

$t_{1/2}$ Approx. 9-15 hours

ROUTES

intravenous

ADMINISTRATION

- Bolus intravenous injection daily twice weekly for 2 weeks (Days 1, 4, 8 & 11), followed by 10 day rest period

DOSINGInjection:

- 1.3 mg/m² IV twice weekly for 2 weeks (Days 1, 4, 8 & 11), followed by 10 day rest period
- Repeat every 3 weeks (usual maximum 8 cycles)
- At least 72 hours between doses

INDICATIONS AND OTHER USES**OTHER ONCOLOGY USES**

Multiple myeloma, disease progression after at least 2 prior courses of treatment

CONTRAINDICATIONS

hypersensitivity to boron or mannitol

SIGNIFICANT INTERACTIONS

no known drug-drug interactions
 Avoid other medications known to cause peripheral neuropathy (e.g. amiodarone, antiviral agents, statins) or decreased blood pressure

DOSE ADJUSTMENT CRITERIAMyelosuppression

If nadir counts ANC $< 0.5 \times 10^3/L$ or platelets $< 25 \times 10^3/L$, **hold dose** until resolved, then **reinstitute** at 25% dose reduction

Neuropathic Pain / Peripheral Sensory Neuropathy

1. Grade 1 with pain/ Grade 2 (interferes with function), **reduce dose** to 1 mg/m²
2. Grade 2 with pain/ Grade 3 (interferes with activities of daily living), **hold dose** until resolved, then **reinstitute at reduced dose** of 0.7 mg/m² given once weekly only
3. Grade 4 (permanent sensory loss that interferes with function), **discontinue treatment**

Renal or Hepatic Dysfunction (Suggested action)

If unexpected elevations in SerCr, liver enzymes, or BUN, **reduce dose**

BORTEZOMIB

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)

nausea (64%), **vomiting** (36%)

- * hypersensitivity, anaphylactic reaction

EARLY ONSET (days to weeks)

- * **thrombocytopenia** (43%, grade 3/4- 30%), **anemia** (32%), **neutropenia**, **pneumonia**, **asthenia** (65%, grade 3/4- 18%), **hypotension**, **dizziness**
- * **diarrhea** (51%, grade 3/4- 7%), **dehydration**

EARLY ONSET (continued)

peripheral neuropathy, **paresthesia & dysesthesia**, **constipation**, **anorexia**, **pyrexia**, **headache**, **arthralgia**, **myalgia**

DELAYED/LATE ONSET

- * cardiac disorders (rare- atrial fibrillation, cardiac arrest, congestive failure, myocardial infarction, pericardial effusion, ventricular tachycardia)
- * DIC (disseminated intravascular coagulation)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Baseline and routine **peripheral neuropathy assessment**
- Measurement of **blood pressure** before and after each dose

SENSORY NEUROPATHY

0. No change

1. Asymptomatic, loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function
2. Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL
3. Sensory alteration or paresthesia interfering with ADL
4. Disabling

SUGGESTED CRITERIA

- Baseline & periodic liver function tests [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels] and **renal function tests** (if failure suspected) [serum creatinine, electrolytes & BUN]
- Assessment for **dehydration**, if diarrhea or vomiting experienced
- Measurement of **blood sugar** in diabetic patients concurrently receiving oral antidiabetic agents
- **Pregnancy test** prior to start of treatment, if woman of childbearing potential

ANTIEMETIC RISK

HIGH RISK (30-90% of patients)

- Use a serotonin receptor antagonist PLUS dexamethasone pre-chemo and post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Intermediate Level-
Not on Canadian market

CDHA Status Non-Formulary
Pharmacare Status Non-Formulary

PHARMACEUTICAL CONSIDERATIONS

Injection: Store unopened vials at room temperature, protect from light. Reconstitute with 3.5 mL sterile Normal saline, to produce a clear, colourless solution. Reconstituted solution may be stored at room temperature for up to 8 hours in the vial or up to 3 hours in a syringe

BUSERELIN

Revision Date: Feb 03

(Antineoplastic Agent, Hormone [Gonadotropin Hormone-Releasing Antigen])

COMMERCIAL PRODUCT DESCRIPTION

Brand Names: Suprefact® Multidose vials with 5.5 mL of solution, Metered dose nasal nebulizer with 10 mL solution - (1.05 mg/mL Buserelin)
 Suprefact Depot® SC Applicator with two Buserelin implant rods (6.6 mg dose)

MECHANISM OF ACTION

Synthetic analog of luteinizing-hormone-releasing hormone (LHRH). Following an initial increase in luteinizing hormone (LH) and follicle stimulating hormone (FSH), chronic administration of buserelin results in a sustained suppression of pituitary gonadotropins. Serum testosterone falls to levels comparable to surgical castration. The exact mechanism of this effect is unknown, but may be related to changes in the control of LH or down-regulation of LH receptors.

PHARMACOKINETICSOral Absorption

none

Distribution

well distributed following subcutaneous injection, trace present in breast milk
 PPB 15%

Metabolism

mainly in plasma
 metabolite(s) active- none known
 inactive- buserelin (5-9) pentapeptide

Excretion

mainly via the kidneys
 urine 67% of intact buserelin at 6-24 hours
 t½ 72-80 minutes

ROUTES

subcutaneous (SC)
 intranasal

EXTRAVASATION HAZARD

none

DOSING*Induction*

- q8h: 500 mcg SC x 7 days

Maintenance

- daily: 200 mcg SC
- tid: 200 mcg (2 sprays) in each nostril (intranasal preparation)
- q2 months: 6.6 mg buserelin acetate (6.3 mg buserelin) depot dose SC
- q3 months: 9.9 mg buserelin acetate (9.45 mg buserelin) depot dose SC
- A delay of a few days is permissible with depot doses

Pediatric: No pediatric indications

Other dosing may be indicated in specific regimens

INDICATIONS AND OTHER USES

- Prostate cancer

OTHER ONCOLOGY USES*Breast cancer***SIGNIFICANT INTERACTIONS**

none reported to date

CONTRAINDICATIONS

- known hypersensitivity to buserelin

SIDE EFFECTS

* may be life-threatening

side effects in **bold**; *italic type* are common**IMMEDIATE ONSET** (hours to days)

hot flushes (72%)
 diarrhea and nausea (1%, SC route)
 reaction at injection site (12%)
 nasal irritation (12%)
 serious disease flare (1%)
 wheal allergy (rare)

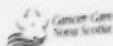
EARLY ONSET (days to weeks)

impotence and loss of libido (75-85%)
headache (29%, nasal route)
 itching (pruritus)

DELAYED/LATE ONSET (weeks- years)

breast swelling and tenderness
 (gynecomastia)

Continued Next Page...

**BUSERELIN****CLINICAL MONITORING**

RECOMMENDED CRITERIA
NO RECOMMENDED TOXICITY
RATINGS

SUGGESTED CRITERIA
NO ADDITIONAL TOXICITY RATINGS

PHARMACEUTICAL CONSIDERATIONSIntranasal solution

1 mg/mL as buserelin acetate in 10 mL glass bottle with metered-dose, spring-loaded pump (nebulizer) provided (100 sprays per bottle). Preserved with benzyl alcohol 1%; also contains sodium chloride to adjust tonicity, sodium hydroxide to adjust pH and citric acid/sodium phosphate buffer. Store below 25°C in the original container. Store in refrigerator or insulated container if temperature exceeds 25°C. do not freeze.

Injection

1 mg/mL (5.5 mL multi-dose vial), as buserelin acetate. Preserved with benzyl alcohol 1%; also contains sodium chloride to adjust tonicity, sodium hydroxide to adjust pH and monobasic sodium phosphate buffer. Store below 25°C in the original container. Store in refrigerator or insulated container if temperature exceeds 25°C. do not freeze.

It is recommended that buserelin not be mixed with other drugs.

Depot Injection

6.6 mg buserelin acetate for 2 month depot, 9.9 buserelin acetate for 3 month depot. Biodegradable rods in ready-to-use applicator with attached needle for SC depot injection. Store syringe in its protective pouch, below 25°C and protected from light and moisture.

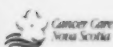
ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level Take Home
Prescription, Depot administration in
Physician's Office (NB. Use of
preprinted Physician Standing Order
is recommended)

CDHA Status

Pharmacare Status

Non-Formulary
Formulary



BUSULFAN

(Antineoplastic Agent, Alkylating Agent)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Myleran® White tablet with 2mg Busulfan

MECHANISM OF ACTION

Reacts with N-7 position of guanosine and interferes with DNA replication and transcription of RNA.

It has a more marked effect on myeloid cells (and is, therefore, useful in the Treatment of CML) than on lymphoid cells. The drug is also very toxic to hematopoietic stem cells. It inhibits little immunosuppressive activity. Interferes with the normal function of DNA by alkylation and cross-linking the strands of DNA.

PHARMACOKINETICS

Oral Absorption

variable; subject to first pass metabolism

Distribution

rapidly eliminated from plasma; crosses placenta

cross blood brain barrier? yes; CSF: plasma ratio is 1:3:1 with BMT doses

Vd adults 0.6-1.0 L/kg; children 1.4-1.6 L/kg PPB 7-55%

Metabolism

extensive hepatic metabolism, to at least 12 metabolites

metabolite(s) active- none known

inactive- 25-35% as methanesulfonic acid

Excretion

primarily as metabolites in urine

urine 10-50% within 24 hours (1-2% unchanged)

Cl adults- 2.5-4.5 mL/min/kg; 95-105 mL/min/m²

older children- 3.0-4.5 mL/min/kg; 90 mL/min/m²

younger children- 6.8-8.4 mL/min/kg; 120-197 mL/min/m²

t½ adults 2.3-2.6 hours; older children 2.7-2.8 hrs; younger children 1.5-2 hrs

SIGNIFICANT INTERACTIONS

acetaminophen, amphotericin, cyclophosphamide, etoposide, itraconazole, phenytoin, succinylcholine, thioguanine
Cytochrome P450 substrate

ROUTES

oral

INDICATIONS AND OTHER USES

- Chronic myelogenous leukemia
- OTHER ONCOLOGY USES (Not Approved)

Leukemias

Multiple myeloma

Myeloproliferative disorders

Non-Hodgkin's lymphoma

Polycythemia rubra vera

CONTRAINDICATIONS

- known hypersensitivity to busulfan
- low WBC, RBC, platelets (myelosuppression)
- pregnancy and breast feeding
- failure to respond to previous courses

PHARMACEUTICAL CONSIDERATIONS

Tablets, 2 mg; store at room temperature (15-30°C); keep dry and protect from light

ANTIEMETIC RISK

- Oral Doses- LOW RISK (Less than 10% of patients)
- No routine antiemetic pre-chemotherapy or post-chemotherapy
- High Doses IV- HIGH RISK (30-90% of patients)
- use a serotonin receptor antagonist PLUS dexamethasone pre-chemotherapy and post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

Continued Next Page...

BUSULFAN

DOSING

Initial

- daily 4-8 mg (range 1-12 mg) po
note: higher doses (eg. 8-12 mg)
should only be used by physicians
experienced with the use of busulfan
daily 0.06 mg/kg or 1.8 mg/m²

Maintenance daily

- 1-3 mg (range 2 mg weekly-4 mg daily)
po intermittent or continuously

Adequate trial

- at least 3 weeks: continuous dosing is
considered when remissions last for
less than 3 months

Bone marrow transplant

- Higher doses are used for tumour
ablation prior to marrow transplant than
for standard treatment regimens. eg. 16
mg/kg po (1 mg/kg q6h x 4 days) may
be used in combination with other
drugs. If vomits less than 30 minutes
after dose and tablets or fragments in
vomit, repeat entire dose. If no
tablets or fragments seen, repeat 50%
of dose. If vomits between 30-60
minutes, repeat 50% of dose.

Pediatric

Initial

daily 0.06 mg/kg or 4 mg/m²

Maintenance

titrate maintenance dose (continuous
or intermittent) to maintain WBC from
15-20 x 10⁹ /L

Bone marrow transplant

16 mg/kg po (1 mg/kg q6h x 4 days). If
vomits less than 30 minutes after dose
and tablets or fragments in vomitus,
repeat entire dose. If no tablets or
fragments seen, repeat 50% of dose. If
vomits between 30-60 minutes, repeat
50% of dose

Other dosing may be indicated in specific regimens

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)

- anaphylaxis (rare)
- increased uric acid levels**
(**hyperuricemia**)
allergic reactions (rash, fever, facial
swelling, joint pain)
nausea, vomiting, diarrhea (rare)
seizures (10% with BMT doses, may be
prevented with phenytoin)

EARLY ONSET (days to weeks)

- low WBC, RBC, platelets**
(**myelosuppression, pancytopenia**)
intermittent use: nadir 11-30 days,
recovery 24-54 days
darkening of skin (5-10%
hyperpigmentation)
hair loss (alopecia, rare)
liver problems (veno-occlusive disease,
25% adults, 8% children with BMT
doses)

DELAYED/LATE ONSET (weeks-years)

- heart problems (endocardial fibrosis,
rare)
- cancer (acute leukemia)
- lung problems (3%)
liver problems (cholestatic hepatitis,
jaundice, rare)
infertility

delayed pubertal development
decreased gonadal function
breast swelling (gynecomastia)
ovarian suppression, amenorrhea,
menopausal symptoms
cataracts (rare, only after long-term use)

Continued Next Page...

BUSULFAN

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Periodic clinical pulmonary exam**, including auscultation, pulmonary toxicity ratings (Cough, SOB)- at follow-up visits

SUGGESTED CRITERIA

- **Periodic liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]

Cough

- 0 None
- 1 Mild
- 2 Moderate
- 3 Severe

Short Of Breath

- 0 No change
- 1 Mild SOB
- 2 Dyspnea on exertion
- 3 Dyspnea at normal level of activity
- 4 Dyspnea at rest

Rated At Follow-up Visit

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level Take Home
Prescription on preprinted
Physician Standing Order,
Specialized Level Capital Health
Only for high dose regimen

CDHA Status Formulary
Pharmacare Status Formulary

CAPECITABINE

(Antineoplastic Agent, Antimetabolite)

Revision Date: Feb 03

DRUG

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Xeloda® Peach-coloured tablets with 150mg or 500mg of Capecitabine

MECHANISM OF ACTION

Prodrug of Fluorouracil (5-FU). It is converted to 5'-deoxy-5-fluorocytidine (DFCR) by carboxylase in the liver. DFCR is converted to 5'-deoxy-5-fluorouridine (DFUR) by cytidine deaminase in the liver and in tumour tissue. DFUR is converted to 5-FU by thymidine phosphorylase. Thymidine phosphorylase is reportedly present in greater amounts in tumor tissue than normal tissue, thus accounting for the "selective" activation of capecitabine. 5-FU is metabolized (anabolic) to active nucleotides intracellularly.

PHARMACOKINETICS

Oral Absorption

readily absorbed; reduced if food taken concurrently

Distribution

tumours, intestinal mucosa, plasma, liver, other tissues
cross blood brain barrier?

Not in animals, humans unknown

PPB: <60%, primarily to albumin (35%)

Metabolism

initially hepatic, hydrolyzed by carboxylesterase to 5'-deoxy-5-fluorocytidine (5 DFCR), which is first converted to 5'-deoxy-5-fluorouridine (5'-DFUR) and then hydrolyzed to the active substance fluorouracil by cytidine deaminase and thymidine phosphorylase metabolite(s) active- fluoruracil & others inactive- yes

Excretion

renal (70%) - 50% as FBAL (a-fluoro-beta-alanine), fecal- 2-6%
urine yes- 95-5% (~3% unchanged)
t½ 45-60 minutes (including active drug)

ROUTES

oral

DOSING

Oral:

3 weeks

- 1250 mg/m² (range 313-1250 mg/m²) PO twice a day for 14 consecutive days starting on day 1 (total dose per cycle 35 000 mg/m² [range 8 764 - 35, 000 mg/m²]).
- For dose level of 1250 mg/m², round dose according to dose calculation table; for other dose levels, round off to the nearest 150 mg.
- Administer within 30 min following the end of a meal.

Pediatric: No pediatric indications
Other dosing may be indicated

INDICATIONS AND OTHER USES

- Breast cancer
- Colorectal cancer

OTHER ONCOLOGY USES

Pancreatic cancer

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

nausea (44%), vomiting (26%)

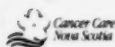
EARLY ONSET (days to weeks)

diarrhea (50%), stomatitis (24%)
abdominal or stomach pain

DELAYED/LATE ONSET (weeks to years)

hand-and-foot syndrome (Palmar-plantar erythrodysesthesia) (45%)
anemia (74%), neutropenia (22%), thrombocytopenia (21%)

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CAPECITABINE

SIGNIFICANT INTERACTIONS

antacids (aluminum/magnesium-containing), coumarin anticoagulants, food, leucovorin, phenytoin, warfarin

CONTRAINDICATIONS

- hepatic function impairment
- history of coronary disease

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Skin assessment**, especially extremities
- Routine assessment of **Diarrhea**, at each clinic visit and telephone reinforcement

Diarrhea

- 0. None
- 1. Increase of 2-3 stools/day over pretreatment
- 2. Increase of 4-6 stools/day or nocturnal stools
- 3. Increase of 7-9 stools/day, incontinence, malabsorption
- 4. Increase of ≥ 10 stools/day, grossly bloody diarrhea, need for parenteral nutrition support

Hand-Foot Skin Reaction

Rated at each visit

- 0. None
- 1. Skin changes or dermatitis without pain
- 2. Skin changes with pain, **not** interfering with function
- 3. Skin changes with pain, interfering with function

SUGGESTED CRITERIA

- Watch for symptoms of fever or infection
- Periodic **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]

DOSE ADJUSTMENT CRITERIA

Hepatic dysfunction

- 1. If Bili=26-51 $\mu\text{mol/L}$ (Grade 2), **HOLD** until Bili $\leq 17 \mu\text{mol/L}$
- 2. If Bili>51 $\mu\text{mol/L}$ (Grade 3), **HOLD** until Bili is normal, then restart at 75% dose or **Discontinue**

Gastrointestinal or Skin Toxicities

- 1. If any Toxicity Score = Grade 2, **HOLD Capecitabine** until score = 0 or 1, resume at 100% dose (if second occurrence, resume at 75% dose, third occurrence at 50%, if fourth occurrence **STOP** Capecitabine)
- 2. If any Toxicity Score = Grade 3, **HOLD Capecitabine** until score = 0 or 1, resume at 75% dose or 1000mg/m² BID (if second occurrence, resume at 50%, if third occurrence **STOP** Capecitabine)
- 3. If any Toxicity Score = Grade 4, **STOP** Capecitabine

ANTIEMETIC RISK

LOW RISK (Less than 10% of patients)

- No routine antiemetic

See Nausea & Vomiting Guidelines for more detail

PHARMACEUTICAL CONSIDERATIONS

Tablets: 150 and 500 mg, inactive ingredients include lactose. Store at room temperature.

Continued Next Page...

CAPECITABINE**GUIDELINES**

Visit the **Cancer Care Nova Scotia** website (www.cancercare.ns.ca) for the guidelines on Capecitabine for the treatment of Breast Cancer and Colorectal cancer

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level: Prescription
ordered on preprinted Physician
Standing Order

Indication restriction- Provincial
Cancer Drug Formulary

CDHA Status Non-Formulary
Pharmacare Status Formulary (red)

NOTE: It is recommended to limit
ordering of this medication to
preprinted Physician Standing Order
form, for patient safety



CARBOPLATIN

(Antineoplastic Agent; Alkylating Agent)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Paraplatin®

Vials with 50mg/5mL, 150mg/15mL and 450mg/45mL solution

Generic products available

Also called CBCDA in some literature

MECHANISM OF ACTION

Alkylating agent. Following intracellular hydrolysis of the "leaving group", the platinum compound binds to DNA, RNA, or proteins.

PHARMACOKINETICS

Oral Absorption

no (4-24%)

Distribution

widely distributed, highest concentration in liver, kidney and skin, tumour tissue;

Excretion in breast-milk unknown

cross blood brain barrier? Yes

Vd 176±5.8 L (normalised to 1.73 m²) (total platinum) PPB

Limited

Metabolism

carboplatin is hydrolyzed to aquated and hydroxylated compounds

metabolite(s) active- Yes

Excretion

primarily in urine, clearance correlates with rate of glomerular filtration

urine 70% of platinum within 24 hours

t_{1/2} α 22±10 minutes t_{1/2} β

1.9±0.2 hours t_{1/2} γ

5.8±1.6 days

(All for total platinum)

Cl 1.38±0.36 L/h (normalized to 1.73 m²) (total platinum)

IV COMPATIBILITY

normal saline, dextrose/saline, 5%

Dextrose

- Concerns about Carboplatin conversion to Cisplatin in Sodium Chloride solutions are not supported by IV admixture studies, where minimal amounts of Carboplatin (<0.7%) were converted to Cisplatin when stored for 24 hours at 25 °C. Either solution is appropriate as diluent for Carboplatin.

ROUTES

intermittent IV (in 100-250 mL over 30-60 minutes)

IV bolus injection

short IV infusion (over 15 min)

ADMINISTRATION

- Mix in 250mL bag (5% Dextrose); Infuse over 30 minutes
- Mix large doses in 500mL bag (5% Dextrose); Infuse over 2 hours

EXTRAVASATION HAZARD

None

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)

- allergic reactions (2%- Symptoms: rashes, pruritis, urticaria, dyspnea and bronchospasm, fever, chills, rigors, hypotension or hypertension, and angioedema)

nausea and vomiting (53%, may be severe)

EARLY ONSET (days to weeks)

- low WBC, RBC, platelets** (myelosuppression, platelet nadir 14-21 days, recovery 35 days, WBC nadir 14-28 days, recovery 42 days)
- kidney problems (25%)
- diarrhea (6%)
- constipation (3%)
- nerve problems (peripheral neuropathy 6%, impaired taste)
- hearing problems (1% tinnitus)

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CARBOPLATIN

SIDE EFFECTS

DELAYED/LATE ONSET

(weeks to years)

liver problems (increase in liver function tests, 33%)

eye problems (visual disturbance, cortical blindness)

DOSING

Intravenous

AUC-based carboplatin dose IV for one dose on day 1

2-4 weeks, AUC = 4-7 IV

Calculate carboplatin dose with Calvert formula:

$$\text{Dose (mg)} = \text{AUC} \times (\text{GFR} + 25)$$

where AUC = 4-7, GFR obtained from nuclear renogram (preferred) or approximated by CrCl calculated from serum creatinine using the Cockcroft-Gault formula:

$$\text{GFR} = \frac{\text{N} \times (140 - \text{Age}) \times \text{weight (kg)}}{\text{serum creatinine (}\mu\text{mol/L)}}$$

where N = 1.04 for females and 1.23 for males

Note that the Cockcroft-Gault formula overpredicts CrCl in certain conditions (eg, muscle wasting, obesity, ascites). Lean or ideal body weight may be used to correct for excess fat or fluid. Repeat renogram to modify dose if > 20% increase in serum creatinine during treatment.

Calvert AUC-based dosing formula is not recommended with GFR or CrCl < 20 mL/min.

3-4 weeks (mg/m²/dosing):

- 300 mg/m² (range 200-400 mg/m²) IV for one dose on day 1

Bone marrow transplant:

higher doses are used for tumour ablation prior to bone marrow transplant, eg,

- 266-666 mg/m²/day IV for 3 days
- 200-500 mg/m²/day IV for 4 days
- 175-400 mg/m²/day IV for 5 days

Pediatric

Intravenous:

Every 3-4 weeks:

400 mg/m² IV once daily for 2 consecutive days starting on day 1 (total dose per cycle 800 mg/m²)

Every 4 weeks:

560 mg/m² IV for one dose on day 1

Every 4 weeks:

80-216 mg/m² IV once daily for 5 consecutive days starting on day 1 (total dose per cycle 400-1080 mg/m²)

Some investigators calculate carboplatin dose with modified Calvert formula:

$$\text{Dose (mg)} = \text{AUC} \times \left[\frac{(\text{GFR} \times \text{BSA})}{1.73} + (15 \times \text{BSA}) \right] \text{ where GFR in mL/min/1.73 and AUC} = 6-7 \text{ OR}$$

$$\text{Dose (mg)} = \text{AUC} \times \{ \text{GFR} + [0.36 \times \text{weight (kg)}] \} \text{ where AUC} = 2-7$$

GFR is obtained from nuclear renogram

Bone marrow transplant:

higher doses are used for tumour ablation prior to bone marrow transplant, eg,

- 100-800 mg/m²/day IV for 3 days
- 250-300 mg/m²/day IV for 4 days
- 250-350 mg/m²/day IV for 5 days

Other dosing may be indicated in specific regimens

NOTE

See Appendix 1 for Dosing Calculations and for standard Carboplatin AUC Dosing Tables

SIGNIFICANT INTERACTIONS

aminoglycoside antibiotics, phenytoin

CARBOPLATIN

INDICATIONS AND OTHER USES

- Ovarian cancer

OTHER ONCOLOGY USES

Brain tumours
Bladder cancer
Breast cancer
Cervical cancer
Endometrial cancer
Ewing's sarcoma
Germ cell tumours
Head and neck cancer
Leukemia, acute lymphocytic
Lung cancer, non-small cell
Lung cancer, small cell
Lymphoma, non-Hodgkin's
Melanoma
Neuroblastoma
Osteosarcoma
Rhabdomyosarcoma
Retinoblastoma
Testicular cancer
Wilms' tumour

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Intermediate Level

CDHA Status	Formulary
Pharmacare Status	Non-Formulary

CONTRAINDICATIONS

- known hypersensitivity to carboplatin or other platinum containing compounds
- pregnancy and breast feeding
- severe renal impairment
- known propensity to cytopenias

ANTIEMETIC RISK

HIGH RISK (30-90% of patients)

- Use a serotonin receptor antagonist PLUS dexamethasone pre-chemotherapy and post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

DOSE ADJUSTMENT CRITERIA

Renal failure

1. If Serum Creatinine = 136-150µmol/L or Creatinine Clearance = 40-60mL/min, reduce dose by 1mg/mL/min (AUC dosing) or by 50mg/m²
2. If Creatinine=151-180µmol/L or Creatinine Clearance = 20-40mL/min, reduce by 2mg/mL/min (AUC dosing) or by 100mg/m²
3. If Creatinine >181µmol/L or Creatinine Clearance <20mL/min, discontinue (Recommended action)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Neurologic toxicity ratings (Sensory) at each visit
- Baseline and routine renal function tests [serum creatinine, electrolytes & BUN]

SENSORY Rated At Each Clinic Visit

- 0 No change
- 1 Mild paraesthesia; no deep tendon reflex
- 2 Mild/moderate sensory loss; moderate paraesthesia
- 3 Sensory loss interferes with function

SUGGESTED CRITERIA

- Periodic liver function tests [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]

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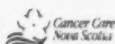
CARBOPLATIN**PHARMACEUTICAL CONSIDERATIONS**

Injection: 50 mg, 150 mg and 450 mg glass vials; each mL contains 10 mg of carboplatin, preservative-free. Store at room temperature. Protect from light.

Diluted solution for infusion: Paraplatin-AQ and Novopharm brand injections: must be further diluted prior to infusion with D5W or NS; the final concentrations should be no less than 0.5 mg/mL; diluted solution is stable for 8 hours at room temperature or 24 hours under refrigeration. Faulding brand injection: must be further diluted with D5W or NS to final concentrations of 0.3-2 mg/mL; diluted solution is stable for 24 hours at room temperature or 48 hours under refrigeration.

Compatibility: The following are compatible via Y-site injection: amifostine, cladribine, filgrastim, fludarabine, granisetron, melphalan, ondansetron, paclitaxel, teniposide, thiotepe, vinorelbine. The following are compatible in the same infusion solution: carboplatin (1 mg/mL) and cisplatin (0.2 mg/mL), carboplatin (1 mg/mL) and etoposide (0.2 mg/mL), carboplatin (1 mg/mL) and ifosfamide (1 mg/mL).

Incompatibility: The following are incompatible in the same infusion solution: carboplatin (10 mg/mL) and fluorouracil (1 mg/mL), carboplatin (1 mg/L) and mesna (1 mg/mL). Aluminum-containing IV needles, syringes or sets should not be used to prepare or administer carboplatin; aluminum reacts with platinum from carboplatin to form a black precipitate, resulting in loss of potency.



CARMUSTINE

(Antineoplastic Agent; Alkylating Agent (Nitrosourea))

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: BiCNU® Vials of 100mg Carmustine for reconstitution with 3mL absolute ethanol (included), then dilution with sterile water to 30mL

Keep refrigerated. DO NOT USE if unopened vial contains liquid or oily film

MECHANISM OF ACTION

A nitrosourea alkylating agent, carmustine inhibits DNA and possibly RNA synthesis. It inhibits key enzyme reactions involved with DNA synthesis, interferes with histidine utilization and the maturation of ribosomal RNA precursors. Carmustine is cell cycle nonspecific, but appears to slow progression from S to G2 phase, and arrest progression through the G2 phase.

PHARMACOKINETICS

Oral Absorption

readily and completely absorbed

Distribution

highly lipid soluble, highest concentration in spleen, liver and ovaries; Excretion in breast-milk unknown cross blood brain barrier? yes, CSF equilibrates within 1 hour to 30-97% of plasma levels

Vd 2.6-3.3 L/kg PPB 80% (in vitro)

Metabolism

rapid and extensive metabolism via hepatic microsomal enzyme oxidation system

metabolite(s) active- Yes

inactive- Yes

Excretion

predominantly by kidneys (60-70%), 6-10% by respiratory excretion, 1% in feces

urine 30% within 24 hours

$t_{1/2} \alpha$ 1.4 minutes $t_{1/2} \beta$ 0.3-1.5

hours Cl 16.7-56 mL/

min/kg

ADMINISTRATION

- Mix in 250mL fluid in polyolefin bag or glass bottle
- (5% Dextrose, Normal Saline)- Use non-PVC equipment & tubing
- Infuse over 60 minutes or longer (2 hours for doses >500mg, or faster infusion, if tolerated)
- Extra IV fluid (up to 750mL) may be run at same time by piggyback, to reduce vein irritation
- If carmustine is being administered peripherally, placing an ice pack intermittently above the injection site in addition to reducing the rate of the infusion may provide some relief of pain and burning along the vein
- **Protect from light**

INDICATIONS AND OTHER USES

- Brain tumours
- Gastrointestinal cancer
- Hodgkin's disease
- Malignant melanoma
- Multiple myeloma
- Non-Hodgkin's lymphomas

OTHER ONCOLOGY USES

Pancreatic cancer

EXTRAVASATION HAZARD

VESICANT (tissue damage on extravasation)

Management stop IV, aspirate, elevate limb, cold intermittent compresses

Follow Extravasation Guidelines

ROUTES

intermittent IV (in 100-250 mL over 1-2 hours or over 15-45 min)

IV COMPATIBILITY

normal saline, dextrose 5%, lactated Ringer's

Continued Next Page...

CARMUSTINE

DOSING

Intravenous:

- q5-8w 150-200 mg/m²
- q6-8w 75-100 mg/m²/day x 2 days
- q6-8w 80 mg/m²/day x 3 days

Elderly/heavily pretreated patients:

- ≥50-75% of usual dose

Bone marrow transplant:

- much higher doses are used for tumour ablation prior to marrow transplantation than for standard treatment regimens, eg. 500-600 mg/m² in 250 mL D5NS over 2 hours

Lifetime dose limits:

- 1400 mg/m² (risk of pulmonary toxicity) careful monitoring is important as pulmonary toxicity may occasionally occur at lower cumulative doses

Pediatric

Initial dose:

- 60 mg/m² or 2 mg/kg IV

Maintenance:

- q6w 30-45 mg/m² or 1-1.5 mg/kg IV

Bone marrow transplant:

- 300-600 mg/m² IV

Other dosing may be indicated in specific regimens

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Clinical pulmonary exam at each visit, including auscultation, pulmonary toxicity ratings (Cough, SOB)
- Watch for symptoms of fever / infection
- Baseline renal function tests (if failure suspected) [serum creatinine, electrolytes & BUN]

Cough

- | | |
|---------------------|---------------------------------------|
| 0 None | 0 No change |
| 1 Mild | 1 Mild SOB |
| 2 Moderate | 2 Dyspnea on exertion |
| 3 Severe | 3 Dyspnea at normal level of activity |
| Rated At Each Visit | 4 Dyspnea at rest |

Short Of Breath

SIDE EFFECTS

* may be life-threatening
side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

- **vein irritation** (phlebitis)
- facial flushing
- **nausea and vomiting** (50%, onset minutes to 2 hours, may be severe)
- heart problems (myocardial ischemia, with high doses)

EARLY ONSET (days to weeks)

- mouth sores (esophagitis)
- diarrhea
- skin discoloration along vein (hyperpigmentation)
- liver problems (26%, reversible, elevated liver function tests)
- kidney problems (glomerular and tubular lesions)
- central nervous system problems (acute encephalopathy with intra-carotid administration, dizziness, loss of balance and ataxia with IV route)

DELAYED/LATE ONSET (weeks- years)

- **low WBC, RBC, platelets** (**myelosuppression**, nadir 25-60 days, recovery 35-85 days)
- liver problems (26%, reversible, elevated liver function tests)
- lung problems (25-30%, mortality 24-80% chronic fibrosis)
- kidney problems (azotemia)
- infertility
- cancer (leukemia)

CUMULATIVE LIFETIME DOSE LIMIT

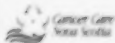
1400mg/m²

SUGGESTED CRITERIA

- Periodic liver function tests [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- Local Site Toxicity ratings, if incident of phlebitis

Local Site Toxicity

- | | |
|----------------------------------|------------------------|
| 0 None | Upon Patient Complaint |
| 1 Pain | Or Clinical Event |
| 2 Pain & inflammation, phlebitis | |
| 3 Ulceration | |
| 4 Plastic surgery | |



CARMUSTINE

CONTRAINDICATIONS

- known hypersensitivity to carmustine
- pregnancy and breast feeding
- low WBC, RBC, platelets (myelosuppression)
- severe renal impairment

ANTIEMETIC RISK

HIGH RISK (30-90% of patients)

- Use a serotonin receptor antagonist PLUS dexamethasone pre-chemotherapy and post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

SIGNIFICANT INTERACTIONS

amphotericin, cimetidine, digoxin, phenytoin, etoposide, metronidazole

DOSE ADJUSTMENT CRITERIA

Renal failure (Suggested action)

Reduce dose by 25-50% if CrCl < 12 mL/min

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-Intermediate Level

CDHA Status Formulary

Pharmacare Status Formulary (red)

PHARMACEUTICAL CONSIDERATIONSInjection

100 mg vial with 3 mL vial absolute alcohol as diluent; protect from light; store in refrigerator. Intact vials are stable at room temperature (below 25°) for up to 7 days but slow decomposition occurs (approximately 3% in 36 days). Because carmustine has a low melting point (29.5-32°C), exposure to these or higher temperatures will cause the drug to liquefy and appear as an oily film in the bottom of the vial; this indicates decomposition and the vials should be discarded.

Reconstitute powder with 3 mL of the supplied diluent (absolute ethanol), then add 27 mL SWI resulting in a final concentration of 3.3 mg/mL in 10% ethanol. To minimize the dose of ethanol administered with high doses (eg, for bone marrow transplantation), 100 mg carmustine may be reconstituted with 1 mL absolute ethanol to a final concentration of 100 mg/mL. Ensure that the carmustine has completely dissolved before withdrawing dose.

Accidental contact of carmustine with the skin has caused transient hyperpigmentation. Immediately wash the affected area thoroughly with soap and water.

Reconstituted solution for injection

3.3 mg/mL solution is clear and colourless or pale yellow. The manufacturer states that the solution should be used immediately after reconstitution and any unused solution discarded. However, Trissel states that the solution is stable in normal fluorescent light for at least 3 hours at room temperature and 24 hours at 4°.

Diluted solution for infusion

Compatible with D5W, NS and 2/3D-1/3NS, with greatest stability at pH 4 and instability at pH above 7. Concentrations of 1.25 mg/mL D5W at room temperature showed loss of 10% in 7.7 hours in a glass container and 18.5% loss in 1 hour in a PVC container. Losses to PVC administration sets have been reported, as much as 23% with a slow infusion rate (eg, 88 mL/hr). Polyethylene-lined infusion sets caused little drug loss, even after 2 hours of static contact with carmustine. It appears that preparation in glass containers and short infusions of 1-2 hours, or infusion through a polyethylene-lined administration set, offer the most stability. If 1 mL absolute ethanol has been used to reconstitute, the final solution should not be used if it is not homogenous or if it contains oily droplets.

Compatible with ondansetron. It is recommended that carmustine not be mixed with other drugs.

CHLORAMBUCIL

(Antineoplastic Agent, Alkylating Agent (Nitrogen Mustard)) Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Leukeran® White tablets with 2mg Chlorambucil

MECHANISM OF ACTION

Chlorambucil is a nitrogen mustard derivative that appears to work as a bifunctional alkylating agent. It probably forms intrastrand cross-links, interfering with DNA replication and RNA transcription and translation. Chlorambucil appears to be cell-cycle nonspecific.

PHARMACOKINETICS

Oral Absorption

yes, bioavailability 70-80%, absorption slowed and decreased 10-20% if ingested with food

Distribution

rapidly cleared from plasma, tissue distribution fairly homogeneous, crosses placenta, found in ascitic fluid. Excretion in breast-milk unknown.

cross blood brain barrier? no information found, but can cause seizures in high doses.

Vd 0.14-0.24 L/kg PPB 99%

Metabolism

predominantly in liver by the hepatic microsomal enzyme oxidation system. metabolite(s) active- phenylacetic acid mustard.

Excretion

Extremely low urinary excretion. Chlorambucil and its metabolites are probably not dialysable.

Urine 15 - 60% of radioactivity appears in urine after 24 hours, less than 1% as intact drug.

t½ 1.5 hours.

2.5 hours, phenyl acetic mustard.

Cl 2.6 ± 0.9 mL/min/kg

DOSE ADJUSTMENT CRITERIA

Hepatic failure

Consider dose reduction if LFTs elevated (eg Bilirubin or AST)

(Suggested action)

SIGNIFICANT INTERACTIONS

amphotericin, cladribine, cyclosporin, food, polio vaccination, succinylcholine

ROUTES

oral

INDICATIONS AND OTHER USES

- Chronic lymphocytic leukemia
- Non-Hodgkin's lymphomas
- Hodgkin's disease
- Mycosis fungoides
- Sezary syndrome

OTHER ONCOLOGY USES

Multiple myeloma

CONTRAINDICATIONS

- known hypersensitivity to chlorambucil (cross-sensitivity to melphalan)
- pregnancy and breast feeding

DOSING

Induction

- daily 0.1-0.15 mg/kg/day
- daily 4.8 mg/day
- daily 0.2 mg/kg/day x 21 days q6w
- q2w 0.4 mg/kg, increase by 0.1 mg/kg every other treatment until mild leukopenia

Maintenance

- may be by reduced daily dose or by intermittent courses of treatment
- daily 0.03-0.1 mg/kg/day
- q4w 1-3 mg/m²

Adequate trial: at least 3 weeks

Pediatric

Induction

daily 0.1-0.2 mg/kg or 4.5 mg/m² x 3-6 weeks, titrate to response/toxicity

Maintenance

daily 0.05-0.1 mg/kg

Other dosing may be indicated



CHLORAMBUCIL

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

- * anaphylaxis (rare)
- increased uric acid levels (hyperuricemia)**
- nausea and vomiting (rare)

DELAYED/LATE ONSET (weeks-years)

- * cancer (acute leukemia, solid tumours)
- eye problems (keratitis)
- * lung problems (chronic fibrosis)
- infertility

EARLY ONSET (days to weeks)

- * **low WBC, RBC, platelets** (**myelosuppression**, nadir 7-14 days, recovery 14-21 days)
- rash
- mouth sores (mucositis, rare)
- double vision (rare)
- liver problems (parenchymal necrosis, rare)
- seizures (rare, with high doses)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC) and serum uric acid levels** before each cycle of treatment
- **Clinical pulmonary exam** at each visit, including auscultation, pulmonary toxicity ratings (Cough, SOB)

Short Of Breath

- 0 No change
- 1 Mild SOB
- 2 Dyspnea on exertion
- 3 Dyspnea at normal level of activity
- 4 Dyspnea at rest

Rated At Periodic Clinic Visits, at Each Visit After 6 Months' Treatment, Or Upon Patient Complaint

SUGGESTED CRITERIA

- Periodic **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)] and serum uric acid

ANTIEMETIC RISK

LOW RISK (Less than 10% of patients)

- No routine antiemetic pre-chemotherapy or post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

PHARMACEUTICAL CONSIDERATIONS

Tablets, 2 mg brown, film-coated, round, store in the refrigerator (2-8° C)

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level Take Home
Prescription on preprinted Physician
Standing Order

CDHA Status Formulary
Pharmacare Status Formulary

NOTE It is recommended to limit ordering of this medication to pre-printed Physician Standing Order form, for patient safety

CISPLATIN

(Antineoplastic Agent; Alkylating Agent)

Revision Date: Feb 03

DRUG

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Platinol® Vials of 10mg/10mL, 50mg/50mL, 100mg/100mL and 50mg/100mL - DO NOT refrigerate

Generic products available

Also called CDDP in some literature

MECHANISM OF ACTION

Cisplatin inhibits DNA synthesis by the formation of DNA cross-links; denatures the double helix; covalently binds to DNA bases and interrupts DNA function; may also bind to proteins; the cis-isomer is 14 times more cytotoxic than the trans-isomer, both forms cross-link DNA but cis-platinum is less easily recognized by cell enzymes and, therefore, not repaired. Cisplatin can also bind two adjacent guanines on the same strand of DNA producing intrastrand cross-linking and breakage

PHARMACOKINETICS

Oral Absorption

no

Distribution

widely distributed with highest levels in kidney, liver and intestines; found in breast milk; distributes into third spaces such as ascites and pleural fluid; may cross the placenta

cross blood brain barrier? trace

Vd 0.17-1.47 L/kg

PPB cisplatin not significantly
inactive metabolites 90%

Metabolism

nonenzymatically transformed to multiple metabolites (inactivated by sulfhydryl groups)

metabolite(s) active- yes (free,
filterable platinum) inactive- yes

Excretion

primarily in urine (>90%); bile (10%)

urine fraction depends on length of
infusion

$t_{1/2} \alpha$ 6-13 minutes $t_{1/2} \beta$ 25-49
minutes $t_{1/2} \gamma$ 2-96 hours

Cl 6.3 mL/min/kg

ADMINISTRATION

DOSES >30mg/m²

- Prehydrate with 500-1000mL Normal Saline with 10mEq/L Potassium Chloride. Infuse over 2 hours
- Prehydration may be given as diluent solution for drug(s) preceding Cisplatin administration
- Mix drug in 500mL Normal Saline; Infuse over 2 hours
- For doses >50mg/m², give 250mL of 20% Mannitol solution (50G Mannitol). Infuse through sidearm concurrent with Cisplatin (may omit by order of physician). May split Mannitol dose as 25G given with prehydration and 25G given concurrent with Cisplatin
- Posthydrate with 500mL Normal Saline (with 10mEq/500mL Potassium Chloride, 2g Magnesium Sulfate may also be added). Infuse over 1 hour

For inpatient administration

- May prehydrate with 1-2L (Normal Saline, NS with 20mEq/L KCl)
- Mix drug in divided doses into 3000mL Normal Saline with 20G Mannitol in each 1L bag; infuse at 125mL/hr over 24 hours
- May posthydrate with 1-1.5L of IV fluid (depending upon renal function, volemia)

See SUPPORTIVE CARE NOTE

ROUTES

direct IV (not recommended)

intermittent IV (low doses eg. 25 mg/m²
in 100 mL over 30 min)

(higher doses in 500-2000 mL over 1-6
hours)

IV COMPATIBILITY

normal saline, dextrose/saline

Continued Next Page...

CISPLATIN

DOSING

To minimize the possibility of inadvertent overdosage it is recommended that written orders for cisplatin specify the intended daily dose rather than the total dose over a period of time. For example, write 25 mg/m²/day for 4 days; do not write cisplatin 100 mg/m² over 4 days.

Infusion:

- q1w: 25 mg/m²
- q2w: 100 mg/m²
- q3-4w: 120 mg/m²
- q2-4w: divided doses from 20-60 mg/m²/day x 2-5 days
- 6-8 mg/m²/day in conjunction with radiotherapy (investigational, can be highly toxic)

Intraperitoneal:

- q1w: 120 mg (increased 30 mg/week until toxicity) x 12 weeks
- q3w: 60-90 mg/m²
- 3w: 270 mg/m² with concomitant IV sodium thiosulfate (eg. 7.5 g/m² load, then 2.13 g/m²/hour x 12 hours)

Intra-arterial:

- q2-5w: 75-150 mg/m² x 1-4 courses

Bone marrow transplant:

- 50 mg/m²/day IV x 3 days

Pediatric:

Intermittent infusion:

- q3w: 60-120 mg/m² IV
- q3w: 3 mg/kg IV (for children <10 kg)

Continuous infusion:

- q7w: 20 mg/m²/day IV x 4 days

Dosage in renal failure:

The usual practice in children is to withhold cisplatin if the GFR is less than 60 mL/min/1.73m²

Other dosing may be indicated in specific regimens

INDICATIONS AND OTHER USES

- Bladder cancer
- Ovarian cancer
- Testicular cancer

OTHER ONCOLOGY USES

Adrenocortical cancer

Brain tumours

Breast cancer

Cervical cancer

Endometrial cancer

Esophageal Cancer

Gastrointestinal cancer

Germ cell tumours

Gestational trophoblastic neoplasia

Gynecological sarcoma

Head and neck cancer

Hepatoblastoma

Hodgkin's Lymphoma

Lung cancer

Malignant melanoma

Neuroblastoma

Non-Hodgkin's lymphoma

Osteosarcoma

Thyroid cancer

Tumors of unknown primary origin

CONTRAINDICATIONS

- known hypersensitivity to platinum compounds
- pregnancy and breast feeding
- low WBC, RBC, platelets (myelosuppression)
- pre-existing renal insufficiency
- hearing impairment

DOSE ADJUSTMENT CRITERIA

Renal failure (Suggested action)

1. If Creatinine Clearance = 30-60mL/min or Serum Creatinine = 136-185µmol/L, **reduce to 50% dose**
2. If Creatinine Clearance < 30mL/min or Serum Creatinine > 185µmol/L, **Omit dose**

CISPLATIN

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)

* anaphylaxis (1-20%, Symptoms- tachycardia, wheezing, bronchoconstriction, hypotension, urticaria and facial edema occurring within a few minutes of administration in previously treated patients. May also include diaphoresis, rhinorrhea, conjunctivitis, generalized erythema, apprehension and a sensation of chest constriction.)

nausea and vomiting (most patients, moderate to severe, onset 1-4 hours, duration 1-7 days)

EARLY ONSET (days to weeks)

* low WBC, RBC, platelets (25-30%, myelosuppression, nadir 18-23 days, recovery 39 days)

kidney problems (28-36%, toxic nephropathy, hypomagnesemia, electrolyte disturbances)

EARLY ONSET (continued)

nausea and vomiting
heart problems (ECG changes, rare)
liver problems (elevated liver function tests, rare)
delayed hypersensitivity reaction (Type II, Symptoms- hemolytic anemia which may sometimes be associated with renal failure)
CNS problems (acute encephalopathy, rare)

DELAYED/LATE ONSET (weeks- years)

nerve problems (peripheral neuropathy)
CNS problems (acute encephalopathy, rare)
eye problems (retinopathy, optic neuropathy)
hearing problems (24%, ototoxicity)
infertility
Raynaud's syndrome (rare)

SIGNIFICANT INTERACTIONS

angiotensin converting enzyme (ACE) inhibitors, aminoglycosides, amphotericin, anticonvulsant drugs, ethacrynic acid, furosemide, lithium, metoclopramide, phenytoin, renally excreted drugs (eg, ifosfamide, high dose methotrexate), many other antineoplastic agents

EXTRAVASATION HAZARD

IRRITANT

Management- stop IV, aspirate, elevate limb, cold intermittent compresses
Follow Extravasation Guidelines

ANTIEMETIC RISK

VERY HIGH RISK (>90% of patients)

- Use a serotonin receptor antagonist PLUS dexamethasone pre-chemotherapy and post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

SUPPORTIVE CARE NOTE

ALL DOSES

- Ensure good urinary output during chemotherapy visit; Patient should void at least once during chemotherapy visit
- Additional hydration may be ordered for hypovolemic patients
- Hydration and diuresis for patients with pre-existing renal, cardiac, or diabetic history at discretion of physician
- Oral hydration with 8 glasses of fluid per day (for 1-2 days) is strongly encouraged; if nausea and vomiting prevent oral hydration, the patient may need to return for more IV hydration

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status- Intermediate Level

CDHA Status

Formulary

Pharmacare Status

Formulary (red)

CISPLATIN

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Baseline and routine renal function tests**- especially if there are other concurrent nephrotoxic drugs [serum creatinine, electrolytes & BUN]
- **Baseline and periodic urine output and urinalysis tests** with high doses
- **Hearing & Neurologic toxicity ratings (Sensory)**- each visit

Hearing

- 0 No change
- 1 Asymptomatic
- 2 Tinnitus
- 3 Correctable hearing loss
- 4 Deafness

Sensory

- 0 No change
- 1 Mild paraesthesia; no deep tendon reflex
- 2 Mild/moderate sensory loss; mod paraesthesia
- 3 Sensory loss interferes with function

Rated At Each Clinic Visit

SUGGESTED CRITERIA

- **Baseline & periodic hearing tests**
- **Serum magnesium levels** with each dose or cycle
- **Periodic liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]

PHARMACEUTICAL CONSIDERATIONS

Injection

0.5 and 1 mg/mL preservative-free solutions, store at room temperature, protected from direct bright sunlight. Freezing may result in a precipitate, which can be redissolved by thawing at room temperature. Do not use solution if the precipitate does not dissolve. A vial of 50 mg of powder is available on an emergency release basis from Bristol-Myers Squibb.

Do not use intravenous needles, syringes or sets that have aluminum components in preparation or administration as aluminum interacts with cisplatin to form a visible black precipitate.

Diluted solution for infusion

Cisplatin requires the presence of chloride ions (at least the equivalent of 0.2% sodium chloride) to remain stable. In solutions with inadequate chloride content, cisplatin decomposes with displacement of one or both of its chloride ions by water. Stable in chloride-containing solutions for at least 24 hours at room temperature. Cisplatin is reported to form complexes with mannitol but these are significant only 2-3 days after mixing. Some mixtures with magnesium sulfate and mannitol or with potassium chloride and mannitol are compatible for at least 48 hours at room temperature. Compatible with ondansetron. It is recommended that cisplatin not be mixed with other drugs. Cisplatin is incompatible with sodium bicarbonate (bright gold precipitate).

CLADRIBINE

(Antineoplastic Agent, Antimetabolite)

Revision Date: Feb 03

DRUG

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Leustatin® Vials of 1mg Cladribine for reconstitution

Also known as 2-chloro-2'-deoxy-β-D-adenosine or 2CDA

MECHANISM OF ACTION

Cladribine is a prodrug that is activated via phosphorylation by deoxycytidine kinase to a 5'-triphosphate form, and incorporated into DNA, inducing DNA strand breaks, shutdown of DNA synthesis, and depletion of nicotinamide adenine dinucleotide (NAD), and adenosine triphosphate (ATP). Effects are seen in resting (G0) as well as dividing cells. The mechanism for killing slowly-dividing cells is uncertain, but may be related to ATP depletion and/or deoxycytidine kinase activity.

PHARMACOKINETICS

Oral Absorption

acid labile, oral bioavailability 55%

Distribution

enters breast-milk

25% of plasma levels cross blood brain barrier

Vd 305 L/m² (pediatrics), 9.2 L/kg

53-160 L/m² (adults) PPB 20%

Metabolism

hepatic, prodrug, activated by intracellular phosphorylation

metabolite(s) active- CdATP

inactive- Yes

Excretion

renal (21-44%); elimination described by two compartment, first-order model

urine 10-30% within 24 hours

t_{1/2} α 3 (20)-35 minutes

t_{1/2} β 6.7 hours

Elimination t_{1/2} 5.4 hours

Cl 36 L/m², 640-978 L/h/kg

ADMINISTRATION

- **Continuous infusion** – mix in 500mL Normal Saline, and infuse over 24 hours, repeat daily for complete dose (usually 96 hours)
- May be given by continuous ambulatory infusion by pump (CADD or Infusor)
- May mix in 250-500mL Normal Saline and administer over 2 hours each day

DOSING

Intravenous:

- once: 0.09-0.1 mg/kg/day x 7 days
- q4-5w: 0.09-0.13 mg/kg/day x 5-7 days
- q4-5w: 4-8.9 mg/m²/day x 5-7 days

Pediatric

Intravenous:

- 6.2-8.9 mg/m²/day x 5 days continuous infusion

Other dosing may be indicated

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

increased uric acid levels
(hyperuricemia)

EARLY ONSET (days to weeks)

* **low WBC, RBC, platelets**

(**myelosuppression**, WBC nadir 7-14

days, recovery 28-56 days, platelet

nadir 7-21 days, recovery 28-42 days)

fever (46% with hairy cell leukemia)

fatigue (45%, 11% >2 weeks)

nausea (28%, usually mild)

headache (22%, 7% >2 weeks)

EARLY ONSET (continued)

rash (5-27%, usually mild, 10% >2 weeks)

injection site reactions (19%)

immunosuppression

DELAYED/LATE ONSET (weeks- years)

kidney problems (renal impairment, rare, 19% with BMT doses)

nerve problems (paraparesis,

quadriparesis, rare, 35% with BMT doses)

Continued Next Page...

CLADRIBINE

INDICATIONS AND OTHER USES

- Hairy cell leukemia

OTHER ONCOLOGY USES

Acute myeloid leukemia
Chronic lymphocytic leukemia
Chronic myelogenous leukemia
Cutaneous T-cell lymphoma
Non-Hodgkin's lymphoma
Waldenstrom's macroglobulinemia

CONTRAINDICATIONS

- known hypersensitivity to cladribine
- pregnancy and breast feeding

SIGNIFICANT INTERACTIONS

amphotericin, chlorambucil, cytarabine

ANTIEMETIC RISK

LOW RISK (Less than 10% of patients)

- No routine antiemetics

See Nausea & Vomiting Guidelines for more detail

ROUTES

intramuscular, direct IV
(not recommended)
intermittent IV (in 2 L NS over 2 hours)
continuous IV
(in appropriate volume over 24 hours)

IV COMPATIBILITY

normal saline

EXTRAVASATION HAZARD

Inadvertent extravasation may be associated with mild erythema, bruising and pain at the administration site. Follow Extravasation Guidelines

DOSE ADJUSTMENT CRITERIA

Renal or hepatic dysfunction: Use with caution. Treatment interruption or discontinuation is recommended if renal toxicity is observed.

Neurotoxicity: Interruption/ discontinuation of treatment if neurotoxicity observed.

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Watch for symptoms of fever or infection

SUGGESTED CRITERIA

- Periodic **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated] If treatment is ongoing
- Baseline **renal function tests** (if failure suspected) [serum creatinine, electrolytes & BUN]
- Infection rating if clinical evidence of opportunistic infection

Infection

- 0 None
- 1 Mild; no active treatment
- 2 Moderate; localized; active treatment required
- 3 Severe; systemic infection; parenteral antibiotics
- 4 Life threatening sepsis

Rated Upon Clinical Indication Of Infection

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status- Advanced Level

Indication restriction- Provincial Cancer Drug Formulary

CDHA Status

Formulary-Restricted- Hematology Guidelines

Pharmacare Status

Non-Formulary

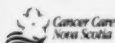
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CLADRIBINE**PHARMACEUTICAL CONSIDERATIONS****Injection**

1 mg/mL clear, colourless solution (10 mL vial); preservative-free. May contain phosphoric acid and/or dibasic sodium phosphate to adjust pH. Store in refrigerator, protected from light during storage. Freezing does not adversely affect the solution but it may result in formation of a soluble precipitate. If freezing occurs, thaw vials to room temperature (do not heat or microwave), shake vigorously to re-solubilize, then store in refrigerator until labelled expiry date. May be frozen and thawed 3 times without affecting stability. The manufacturer recommends that unused portions of vials be disposed since they contain no preservatives.

Diluted solution for infusion

For 24-hour continuous infusion, dilute daily dose in up to 1 L NS. D5W is not recommended as a diluent because of increased degradation of cladribine. Dilutions in NS may be stored in PVC containers, refrigerated and protected from light, for up to 8 hours before administration and are physically and chemically stable at room temperature under fluorescent light for at least 24 hours. For 7-day continuous infusion, dilute dose to 100 mL in bacteriostatic NS (benzyl alcohol preserved). The manufacturer recommends passing both the drug and the diluent through a 0.22 micron filter to minimize the risk of microbial contamination. Dilutions in bacteriostatic NS may be stored, refrigerated and protected from light, for up to 8 hours before administration and have shown acceptable physical and chemical stability for at least 7 days in Pharmacia Deltec Medical Cassettes®. It is recommended that cladribine not be mixed with other drugs.



CYCLOPHOSPHAMIDE

(Antineoplastic Agent; Alkylating Agent (Nitrogen Mustard)) *Revision Date: Feb 03*

COMMERCIAL PRODUCT DESCRIPTION

Brand Names: Cytoxan® Tablets of 25mg & 50mg- White with blue specks;
Vials of 1000mg & 2000mg

Procytox® Coated tablets of 25mg & 50mg;
Vials of 200mg, 500mg, 1000mg & 2000mg

MECHANISM OF ACTION

Cyclophosphamide is an alkylating agent that prevents cell division by cross-linking DNA strands and decreasing DNA synthesis. It is a cell cycle phase nonspecific agent. It also possesses potent immunosuppressive activity. Prodrug, that must be metabolized to active metabolites in the liver.

PHARMACOKINETICS

Oral Absorption

yes, bioavailability 75-100%

Distribution

most tissues, crosses placenta, present in breast milk, present in ascites
cross blood brain barrier? Yes
Vd 0.48-0.71 L/kg PPB 10-56%

Metabolism

mainly activated by hepatic microsomal enzyme oxidation system, some activation peripherally; great interpatient variability in metabolism
metabolite(s): active- acrolein, 4-aldophosphamide, nor-nitrogen-mustard, 4-hydroperoxycyclophosphamide
inactive- Yes

Excretion

drug and metabolites excreted by kidney, tubular reabsorption occurs
urine 37-82% (20-45% of that is unchanged)
t½ 4-10 hours adults; 1-6.5 hours children
Cl 1.3 mL/min/kg, 43-160 mL/min, 47-90 mL/min/m²

SIGNIFICANT INTERACTIONS

alcohol, allopurinol, antidiabetic agents, benzodiazepines, chloramphenicol, cimetidine, corticosteroids (eg, dexamethasone, prednisone), dapsone, digoxin, morphine, phenobarbital, phenytoin, succinylcholine, warfarin, thiazide diuretics, other antineoplastic agents

IV COMPATIBILITY

normal saline, dextrose 5%, lactated Ringer's, mesna

ROUTES

oral
direct IV (100 mg/minute)
intermittent IV (over 20-60 minutes, BMT 2 hours)
continuous IV (in convenient volume)

ANTIEMETIC RISK

Oral Doses-INTERMEDIATE RISK (10-30% of patients)

- Use a dexamethasone pre-chemotherapy and a dopamine receptor antagonist PRN post-chemotherapy

IV Doses- HIGH RISK (30-90% of patients)

- Use a serotonin receptor antagonist PLUS dexamethasone pre-chemotherapy and post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

EXTRAVASATION HAZARD

none

DOSE ADJUSTMENT CRITERIA

Renal failure (Suggested action)
Give **75%** of dose if CrCl = 10-50 mL/min
Give **50%** dose if CrCl < 10mL/min- especially for large intravenous doses

Continued Next Page...

CYCLOPHOSPHAMIDE

ADMINISTRATION

- Mix doses $\leq 1000\text{mg}$ in 100mL bag (5% Dextrose, Normal Saline); Infuse over 30 minutes
- Doses $< 1000\text{mg}$ may be given by direct IV push at $< 100\text{mg}/5\text{mL}$ per minute, followed by a Normal Saline flush, if no IV line has been set up (*administering nurse should be certified to administer IV push chemotherapy agents*)
- Mix doses $> 1000\text{mg}$ in 250-500mL bag (5% Dextrose, Normal Saline); Infuse over 30-60 minutes
- Doses $> 2000\text{mg}$ may be mixed in 250-500mL bag (5% Dextrose, Normal Saline); Infuse over 30-60 minutes
- Larger doses of drug should be given with larger total fluid volumes to the patient; patients receiving doses $>> 1000\text{mg}$ should receive at least 500-750mL total fluid, either as oral or IV hydration
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration
- Inadequate total hydration may result in dose-related hemorrhagic cystitis
- Mesna may be useful in the prevention of urinary tract toxicity. Mesna is usually given as an IV bolus, equal to 20% of the cyclophosphamide dose at 0, 4 and 8 hours after cyclophosphamide. The injectable form of mesna may also be given orally as 40% of the cyclophosphamide dose at 0, 4 and 8 hours after cyclophosphamide. However, mesna is poorly tolerated as an oral drug as it has an unpleasant taste and odor. The palatability of mesna may be increased by mixing the dose in juice, cola or milk and by drinking the solution through a straw.

DOSING

Oral:

- daily: 1-5 mg/kg continuously, titrated to response/toxicity
- daily: 60-120 mg/m²
- q2-4w: 40-50 mg/kg x 1 dose or divided over 2-5 days
- q4w: 200 mg/m²/day x 4 days
- Oral preparations may be prepared by dissolving cyclophosphamide for injection in Aromatic Elixir USP to a concentration of 1-5 mg/mL.

Intravenous:

- biw: 3-5 mg/kg (biw = twice a week)
- q7-10d: 10-15 mg/kg
- q2-4w: 40-50 mg/kg x 1 dose or divided over 2-5 days
- q3-4w: 10-20 mg/kg/day x 2-5 days
- q3-4w: 500-1500 mg/m²
- q4w: 400 mg/m²/day x 5 days

Other dosing may be indicated in specific regimens

Bone marrow transplant:

- much higher doses are used for tumour ablation prior to marrow transplant than for standard treatment regimens; eg, 1.8-2.4 g/m²/day IV for 2-4 days or 50-90 mg/kg/day IV x 1-4 days may be used in combination with other cytotoxic drugs

Compromised bone marrow:

- decrease dose by 30-50%

Pediatric Bone marrow transplant:

50-60 mg/kg/day IV x 2-4 days or 1.2-1.8 g/m²/day IV x 3-4 days.

NOTE: Children with Fanconi's anemia are particularly sensitive to the toxic effects of cyclophosphamide used prior to bone marrow transplantation and doses are approximately 25% of the usual pre-transplant dose used for other indications;

eg, 5-10 mg/kg/day IV x 4 days

CYCLOPHOSPHAMIDE

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Urinalysis (RBCs)**- routine for high intravenous doses ($>1000\text{mg/m}^2$); periodic for low IV dose/oral doses, and in response to patient complaint
- **Baseline renal function tests** (if failure suspected) [serum creatinine, electrolytes & BUN]

SUGGESTED CRITERIA

- Cystitis toxicity rating if patient complaint of symptoms
Cystitis
 - 0. None
 - 1. Mild symptoms
 - 2. Symptoms relieved with therapy
 - 3. Symptoms not relieved
 - 4. Life-threatening
- Rated At Each Clinic Visit For Doses $>1000\text{mg/m}^2$**

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)

- anaphylaxis (rare)
facial burning, nasal stuffiness (during administration)
- **nausea and vomiting** (onset 6-12 hours, duration 24-36 hours)
- injection site problems (chemical phlebitis)
- increased uric acid levels (hyperuricemia)
- bladder problems (10%, BMT $>40\%$, hemorrhagic cystitis)
- kidney problems (SIADH, hyponatremia)
- skin problems (radiation recall reaction, rare)

EARLY ONSET (days to weeks)

- **low WBC, RBC, platelets** (**myelosuppression**, nadir 8-15 days, recovery 17-28 days)
- **hair loss** (reversible alopecia, 3-6 weeks after start of therapy)
- **loss of appetite (anorexia)**
- Cardiotoxicity (especially with high dose cyclophosphamide)- may be severe or fatal congestive heart failure (ie. hemorrhagic myocarditis) within a few days of therapy
- mouth sores (rare, stomatitis)
- skin problems (radiation recall reaction, rare; hyperpigmentation of skin or fingernails)
- lung problems (interstitial pneumonitis)
- heart problems (hemorrhagic necrosis, with BMT doses, rare)

DELAYED/LATE ONSET (weeks to years)

- * bladder problems (hemorrhagic cystitis)
- * lung problems (interstitial pneumonitis, pulmonary fibrosis)
- * fertility problems (amenorrhea, azospermia, infertility)
- * cancer (secondary malignancies)

CONTRAINDICATIONS

- known hypersensitivity to cyclophosphamide
- pregnancy and breast feeding
- low WBC, RBC, platelets (myelosuppression)
- bladder problems (hemorrhagic cystitis) on treatment
- lung problems (pulmonary fibrosis or pneumonitis) on treatment

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CYCLOPHOSPHAMIDE

INDICATIONS AND OTHER USES

- Breast cancer
- Lung cancer, small cell
- Multiple myeloma
- Mycosis fungoides
- Neuroblastoma
- Ovarian cancer
- Bone marrow transplant conditioning protocols

Lung cancer, non-small cell
Non-Hodgkin's lymphoma
Osteogenic sarcoma
Retinoblastoma
Rhabdomyosarcoma
Soft tissue sarcoma
Testicular cancer

OTHER ONCOLOGY USES

Acute lymphocytic leukemia
Acute myelogenous leukemia
Brain tumours, pediatric
Chronic lymphocytic leukemia
Chronic myelogenous leukemia
Endometrial cancer
Ewing's sarcoma
Germ cell tumours
Hodgkin's disease

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Injection-Basic Level,
Oral-Community Level. Take home
 prescription on preprinted Physician
 Standing Order (PSO)

CDHA Status Formulary
 Pharmacare Status Formulary

NOTE: Recommended to order on
 preprinted Physician Standing Order
 form, for patient safety

PHARMACEUTICAL CONSIDERATIONS

Tablets

25 mg, 50 mg, store at room temperature. The Procytox® brand is coated and contains lactose. Procytox® 25 mg tablets contain tartrazine.

Injection

200 mg, 500 mg, 1 g and 2 g vials, store at room temperature.
 Reconstitute powder with SWI or BWI (benzyl alcohol- or paraben-preserved) to a final concentration of 20 mg/mL. Heating should not be used to facilitate dissolution. avoid the use of benzyl alcohol-preserved BWI in children less than 2 months of age. Powder may be taken orally by dissolving in Aromatic Elixir USP. Such a solution should be kept refrigerated and used within 16 days of preparation.

Reconstituted solution for injection

Clear, colourless solution; physically stable 6 days when refrigerated but manufacturers recommend immediate use when reconstituted without preservatives. Trissel cites a reference indicating a stability of at least 4 weeks when stored in glass containers under refrigeration.

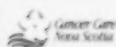
Stability in syringes

Trissel cites a reference indicating that a 20 mg/mL solution is stable in polypropylene syringes for 4 weeks at 4°C. It is also stable for 19 weeks when frozen but the syringe itself may not be able to withstand such storage conditions.

Diluted solution for infusion

Compatible with D5W, NS, dextrose-saline combinations and lactated Ringer's. No more than 1.5% decomposition was seen in 8 hours at room temperature and 6 days under refrigeration in dextrose and dextrose-saline combinations. Solutions in NS in PVC bags showed only 3.5% decomposition in 24 hours at room temperature and no loss in 4 weeks under refrigeration.

Compatible with mesna in D5W or lactated Ringer's for 24 hours, also with ondansetron. It is recommended that cyclophosphamide not be mixed with other drugs.



CYPROTERONE

(Antiandrogen)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Androcur® White tablets with 50mg Cyproterone
 Androcur Depot® Ampuls with 100mg Cyproterone in castor oil

MECHANISM OF ACTION

Steroid which clinically demonstrates 2 distinct properties:

Antiandrogenic: Cyproterone blocks the binding of dihydrotestosterone (active metabolite of testosterone) to the specific receptors in the prostatic carcinoma cells).

Progesteric/antigonadotrophic: Cyproterone exerts a negative feed-back on the hypothalamo-pituitary axis, by inhibiting the secretion of LH leading to diminished production of testicular testosterone.

PHARMACOKINETICS

Oral Absorption

oral absorption complete at 50 mg dose

Distribution

tissue distribution is one of the major causes of the rapid fall of plasma levels

Metabolism

the principle metabolite is 15 B-hydroxy-cyproterone acetate

metabolite(s) active- no information
 inactive- yes

Excretion

drug is excreted unchanged in urine and feces

urine 33% feces 60%
 t_{1/2} 38 ± 5 hours (oral route); 38 ± 14 hours (IM route)

ROUTES

IM, po

DOSING

Oral

- bid: 50 mg taken after meals with diethylstilbestrol (DES) 0.1 mg daily
- bid: 100 mg as single agent or post orchidectomy

Intramuscular

- q1-2w: 300 mg

Pediatric: No pediatric indications

Other dosing may be indicated

EXTRAVASATION HAZARD

none

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)
 nausea and vomiting

EARLY ONSET (days to weeks)
 breast swelling or soreness (gynecomastia)
 discharge from the nipple (galactorrhea)
impotence or decreased sex drive (decreased libido)
 blood clots (thrombophlebitis)
 swelling of hands, feet or lower legs (edema)
 elevated liver function tests
 bowel changes (diarrhea or constipation)

EARLY ONSET (continued)
 fatigue, lethargy, weakness
 increased serum calcium levels (hypercalcemia)
 loss of diabetic control
 hypochromic anemia (rare)

DELAYED/LATE ONSET (weeks- years)
 elevated liver function tests
 depression
 low sperm counts
 benign breast lumps (benign nodular hyperplasia of the breast)
 dry skin

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CYPROTERONE

INDICATIONS AND OTHER USES

Prostate cancer

SIGNIFICANT INTERACTIONS

*ethinyl estradiol

CONTRAINDICATIONS

- severe liver or kidney dysfunction
- known hypersensitivity to cyproterone

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Baseline & periodic **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]

SUGGESTED CRITERIA

NO ADDITIONAL TOXICITY RATINGS

PHARMACEUTICAL CONSIDERATIONS

Depot injection

100 mg/mL (3 mL ampul) cyproterone acetate in castor oil solution. Store at room temperature.

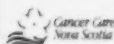
Tablets

50 mg cyproterone acetate, store at room temperature. Contain corn starch and lactose. Tartrazine- and gluten-free.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level Take Home
Prescription (NB. Use of preprinted
Physician Standing Order is
recommended)

CDHA Status	Non-Formulary
Pharmacare Status	Formulary



CYTARABINE

(Antineoplastic Agent, Antimetabolite)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name:

Cytosar®

Vials with 100mg, 500mg, 1000mg & 2000mg for reconstitution

Generic Name

Vials with 100mg/1mL & 500mg/5mL

MECHANISM OF ACTION

Inhibition of DNA synthesis. Cytosine gains entry into cells by a carrier process, and then must be converted to its active compound, aracytidine triphosphate. Cytosine is a purine analog and is incorporated into DNA, the primary action is inhibition of DNA polymerase resulting in decreased DNA synthesis and repair. The degree of cytotoxicity correlates linearly with incorporation into DNA that is responsible for drug activity and toxicity.

Cytarabine is specific for the S phase of the cell cycle.

PHARMACOKINETICS

Oral Absorption

poorly absorbed from gastrointestinal tract, <20% bioavailability

Distribution

rapidly and widely distributed, crosses the placenta, Excretion in breast-milk unknown

cross blood brain barrier? CSF:

plasma ratio 14% (rapid IV), 40-60% (infusion or SC)

Vd 3±1.9 L/kg PPB 13%

Metabolism

rapid and extensive metabolism by cytidine deaminases mainly in liver and kidneys

metabolite(s) active- cytosine arabinoside triphosphate inactive- uracil arabinoside

Excretion

Renal clearance accounts for less than 10% of total clearance. Clearance of IT dose is by CSF bulk flow and diffusion to

ROUTES

subcutaneous (rotate sites, may give continuous infusion)

intramuscular (rotate sites)

direct IV (recommended for higher doses)

intermittent IV (over at least 1 hour)

continuous infusion (over 1-24 hours)

intrathecal (in 6 mL, range 5-15 mL, preservative-free solution, may remove equal volume CSF first)

INDICATIONS AND OTHER USES

- Acute myelogenous leukemia
- Meningeal leukemia
- Acute lymphocytic leukemia
- Chronic myelogenous leukemia
- Erythroleukemia
- Non-Hodgkin's lymphoma

CONTRAINDICATIONS

- known hypersensitivity to cytarabine
- pregnancy and breast feeding

ANTIEMETIC RISK

HIGH RISK (30-90% of patients)

- Use a serotonin receptor antagonist PLUS dexamethasone pre-chemotherapy and post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

IV COMPATIBILITY

normal saline, dextrose 5%, lactated Ringer's

SIGNIFICANT INTERACTIONS

acyclovir, amphotericin, anticonvulsants, cyclosporin, flucytosine, gentamycin, digoxin, alkylating agents, purine analogs, methotrexate, other antineoplastic agents

EXTRAVASATION HAZARD

none

Continued Next Page...

CYTARABINE

DRUG

Induction:

- q2w 200 mg/m²/day x 5 days - continuous infusion
- q2-4w 100 mg/m²/day x 7-10 days - continuous infusion
- 100 mg/m² q12h x 7 days - rapid injection
- 2-6 mg/kg/day x 5-10 days - continuous infusion or in 2-3 divided doses - rapid injection
- daily 100-200 mg/m² until remission

Maintenance:

- q1-4w 1-1.5 mg/kg IM/SC
- q4w 70-200 mg/m²/day x 2-5 days - continuous infusion or rapid injection

Intrathecal:

- daily 5-75 mg/m² or 25-100 mg x 4-5 days
- biw 50 mg in 6 mL NS alternating with methotrexate twice weekly x 6 doses (ie. 3 doses of each over 3 weeks)
- q3d until CSF cleared, then q7d until 6 doses after last positive CSF sample
- biw 50 mg in 6 mL NS alternating with methotrexate twice weekly until CSF cleared, then q1w x 6 doses, then q1m x 3 doses
- q3-4w with each cycle of systemic therapy x 6 doses

DOSING

High dose:

- q2-3w 2-3 g/m² over 1-3 hours q12h x 4-12 doses

Bone marrow transplant

- much higher doses are used for tumour ablation prior to marrow transplant than for standard treatment regimens; eg. 3 g/m² loading dose over 2 hours, then 1.5 g/m²/day x 3 days may be used in combination with other cytotoxic drugs

Pediatric

Intravenous:

- q4w 75-150 mg/m²/day or 5 mg/kg/day x 5 days
- biw 300 mg/m²/day (biw = twice weekly) x 4 weeks
- q4w 150 mg/m²/day x 5 days by continuous IV or SC infusion
- 1-3 g/m²/dose q12h x 4-12 doses (<3 years: 100 mg/kg/dose)

Intrathecal:

- <1 year: 20 mg
- 1-2 years: 30 mg
- 2-3 years: 50 mg
- >3 years: 70 mg

Bone marrow transplant

- 3 g/m²/dose IV q12h x 12 doses

Other dosing may be indicated in specific regimens

ADMINISTRATION

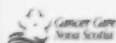
- May be given as IM or SC injection

Intravenous

- May be mixed in 50-100mL minibag (Normal Saline); Infuse over 15-30 minutes
- Doses >1g may be mixed in 500mL bag (5% Dextrose, Normal Saline); Infuse over 2-3 hours
- May be given by direct IV push, followed by a Normal Saline flush, if no IV line has been set up (*administering nurse should be certified to administer IV push chemotherapy agents*)
- Continuous infusion using ambulatory infusion pump. Infuse through central venous access device

For inpatient administration:

- Mix dose in 1000mL Normal Saline, infuse over 24 hours
- Intrathecal
- Reconstitute powder with preservative-free 0.9% Sodium Chloride, or use preservative-free solution, use solution immediately



CYTARABINE

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

Parenteral Cytarabine- Lower Doses

IMMEDIATE ONSET (hours to days)

- * anaphylaxis (rare- Symptoms: dyspnea, chest pain, fever, angioedema, urticaria and hypotension)
- increased uric acid levels (hyperuricemia)**
- nausea and vomiting**
- Cytarabine syndrome: acute reaction with fever, rigors, diaphoresis, myalgia, arthralgia, maculopapular rash, conjunctivitis, malaise, chest pain and hypotension. Occurs 6-12 hours after administration
- flu-like syndrome
- injection site problems (thrombophlebitis, pain, inflammation, rare)

EARLY ONSET (days to weeks)

- * **low WBC, RBC, platelets (myelosuppression)**, first nadir 7-9 days, second nadir 15-24 days, recovery 25-34 days)
- * lung problems (pulmonary edema)
- eye problems (conjunctivitis)
- mouth sores (stomatitis)**
- hair loss (alopecia, more common with high doses)
- * gastrointestinal problems (hematemesis, diarrhea, abdominal pain)
- liver problems (elevated liver function tests, hepatotoxicity)
- nerve damage (peripheral neuropathy, rare)
- skin problems (rash, freckling)
- blood problems (megaloblastosis)

DELAYED/LATE ONSET

infertility

Intrathecal Cytarabine

IMMEDIATE ONSET (hours to days)

- nausea and vomiting**
- headache (transient)**
- mild fever**

EARLY ONSET (days to weeks)

- CNS toxicity (chemical arachnoiditis, meningism, paresthesia, paraplegia, spastic paraparesis, seizures (all very rare; associated with cytarabine in combination with IV chemotherapy and radiotherapy)

High Dose Cytarabine (same adverse effects as lower dose Cytarabine, PLUS)

IMMEDIATE ONSET (hours to days)

- * CNS problems (cerebellar toxicity 7-28%- horizontal nystagmus and ataxia, dysarthria, dysidiadochokinesia, intention tremors, cerebral dysfunction- somnolence, confusion, disorientation, headache, memory loss, cognitive dysfunction, occasionally seizure activity, coma, personality changes)
- * sudden respiratory distress, progressing to pulmonary edema & cardiomegaly
- peripheral motor & sensory neuropathies
- diffuse interstitial pneumonitis- rare
- pancreatitis- rare

EARLY ONSET (days to weeks)

- * syndrome of inappropriate secretions of antidiuretic hormone (SIADH)- rare
- * severe GI ulceration
- * cardiomyopathy
- * bowel necrosis, necrotizing colitis
- * sepsis
- * liver abscess
- hemorrhagic conjunctivitis, reversible corneal toxicity (keratitis)

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CYTARABINE

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum uric acid levels before each cycle of treatment

SUGGESTED CRITERIA

- Baseline & periodic liver function tests [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]

PHARMACEUTICAL CONSIDERATIONS

Injection

100 mg, 500 mg, 1 g, 2 g vials and a 100 mg/mL aqueous solution; preservative-free; store at room temperature.

Reconstitute powder with NS as follows:

100 mg vial with 2 mL to final concentration of 50 mg/mL with 5 mL to final concentration of 20 mg/mL

500 mg vial with 10 mL to final concentration of 50 mg/mL

1 g vial with 10 mL to final concentration of 100 mg/mL

2 g vial with 19 mL to final concentration of 100 mg/mL

For IV or SC use, BWI (benzyl alcohol-preserved) may be used to reconstitute 100 mg or 500 mg vials. For high-dose IV therapy, only preservative-free NS should be used to reconstitute. For intrathecal use, only preservative-free NS, Elliott's B solution or the patient's own spinal fluid should be used to reconstitute. The 100 mg/mL aqueous solution is not suitable for intrathecal use without further dilution.

Reconstituted solution for injection

Solutions reconstituted with BWI may be stored for 48 hours at room temperature (15-30°C). Solutions reconstituted with preservative-free diluents should be used immediately. The manufacturer of the 100 mg/mL aqueous solution recommends discarding unused portions of vials within 24 hours of puncture. Any solution of cytarabine should be discarded if it becomes hazy. One reference indicates that solutions reconstituted with BWI are stable in plastic syringes for at least 7 days at room temperature or refrigerated.

Diluted solution for infusion

The manufacturers recommend that further dilutions in NS, D5W, lactated Ringer's or SWI should be used within 24 hours if stored at room temperature or within 72 hours if refrigerated. However, solutions of 2, 6 and 8 g in 250 mL D5W or NS in (Travenol) glass bottles and (Vialflex) PVC bags have been shown to be chemically stable for 7 days at room temperature.

Cytarabine 10-100 mcg/mL showed no loss to either Millex-OR or Millex-FG filters. It is recommended that cytarabine not be mixed with other drugs although there is conflicting evidence of compatibility with some drugs. Specific references should be consulted for compatibility before combining cytarabine and another drug.

DOSE ADJUSTMENT CRITERIA

Renal dysfunction (Suggested action)

No adjustment required (except for high dose protocols in which patients may experience increased neurotoxicity).

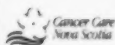
Hepatic dysfunction adjustment required (no details available)

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Basic Level for low dose;

Advanced Level for high dose or intrathecal dose

CDHA Status Formulary
Pharmacare Status Formulary (red)



DACARBAZINE

(Antineoplastic Agent, Alkylating Agent)

Revision Date Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name DTIC® Vials with 200mg for reconstitution with 19.7mL sterile water for injection

MECHANISM OF ACTION

The exact mechanism of action is unknown, although it appears to act as an alkylating agent, forming methylcarbonium ions that attack nucleophilic groups on DNA. It appears to inhibit DNA, RNA, and proteins synthesis by cross-linking DNA strands. Although it is a structural analog of 5-aminoimidazole-4-carboxamide, a purine precursor, it does not appear to inhibit purine synthesis. It is active in all phases of cell cycle.

PHARMACOKINETICS

Oral Absorption

erratic, slow and incomplete

Distribution

liver; excretion in breast-milk unknown
cross blood brain barrier? <15%

Vd 0.63-1.49 L/kg PPB 20%

Metabolism

activated by hepatic microsomal enzyme oxidation system

metabolite(s) active- yes- MTIC
[(methyl-triazene-1-yl)-imidazole-4-carboxamide]

inactive- amino imidazole carboxamide (AIC, major)

Excretion

subject to renal tubular secretion, 50% as unchanged DTIC and 9% to 18% as metabolite; minor hepatobiliary and pulmonary

urine 30-45% in 6 hours

t_{1/2α} 3 minutes t_{1/2β} 41 min

Cl 15.4 mL/kg/min

IV COMPATIBILITY

normal saline, dextrose 5%

ROUTES

direct IV (not recommended, painful)
intermittent IV (in 250-500 mL over 15-60 minutes)

ADMINISTRATION

- May be given by slow infusion through sidearm of free-flowing IV (5% Dextrose, Normal Saline)
- May be mixed in 250-500mL bag (5% Dextrose, Normal Saline); Infuse through main IV line or central venous access device, with an additional 500mL Normal Saline run at same time by piggyback, to reduce vein irritation (more IV fluid if ordered by physician)
- Infuse over 30 to 60 minutes (up to 120 minutes if vein irritation)
- If vein irritation, infuse slowly
- **PROTECT FROM LIGHT**

DOSING

Intravenous:

- q14d 375 mg/m²
- q3-4w 850 mg/m²
- q3-4w 250 mg/m²/day x 5 days
- q3w 2-4.5 mg/kg/day x 10 days
- q4-6w 650-1450 mg/m² (extreme nausea and vomiting)

Pediatric

Intravenous:

- q2w 375 mg/m²
- q3-4w 150-250 mg/m²/day x 5 days
- q6-8w 750 mg/m²

Other dosing may be indicated in specific regimens

SIGNIFICANT INTERACTIONS

interleukin-2, levodopa, phenobarbital, phenytoin, other antineoplastic agents

Continued Next Page...

DACARBAZINE

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

- * anaphylaxis (rare)
- vein irritation** (pain, phlebitis)
- nausea and vomiting** (90%, duration 1-12 hours)
- diarrhea (rare)
- skin problems (facial flushing, facial paresthesia, photosensitivity, rare)
- CNS toxicity: Confusion, lethargy, blurred vision, seizures, headache and polyneuropathy- during therapy

EARLY ONSET (days to weeks)

- * **low WBC, RBC, platelets (myelosuppression)**, nadir 16-28 days, recovery 21-35 days)
- * allergy-mediated hepatotoxicity (allergic thrombophlebitis with secondary hepatic necrosis)
- flu-like symptoms (10%, onset 7 days, duration 7-21 days)
- * liver problems (rare, elevated liver function tests, venocclusive disease, allergic vasculitis)
- kidney problems (increased BUN, renal impairment, rare)
- hair loss (rare, reversible alopecia)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment

Local Site Toxicity

0. None
1. Pain
2. Pain & inflammation, phlebitis
3. Ulceration
4. Plastic surgery

Upon Patient Complaint Or Clinical Event

SUGGESTED CRITERIA

- Baseline & periodic **liver function tests** (if failure suspected) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- Baseline & periodic **renal function tests** (if failure suspected) [serum creatinine, electrolytes & BUN]
- Local Site Toxicity ratings, if incident of phlebitis

INDICATIONS AND OTHER USES

- Malignant melanoma

OTHER ONCOLOGY USES

Hodgkin's disease

Neuroblastoma

Soft tissue sarcomas

ANTIEMETIC RISK

HIGH RISK (30-90% of patients)

- Use a serotonin receptor antagonist PLUS dexamethasone pre-chemotherapy and post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

CONTRAINDICATIONS

- known hypersensitivity to dacarbazine
- pregnancy and breast feeding
- low WBC, RBC, platelets (myelosuppression)
- severe liver failure

EXTRAVASATION HAZARD

IRRITANT

Management- stop IV, aspirate, elevate limb, cold intermittent compresses
Follow Extravasation Guidelines

Continued Next Page...

DACARBAZINE**PHARMACEUTICAL CONSIDERATIONS****Injection**

200 mg: contains citric acid to enhance solubility. Store in refrigerator, protected from light. One reference (Dalton-Bunnow) states that dacarbazine is stable for 4 weeks at room temperature.

Reconstitute powder with 19.7 mL SWI to a final concentration of 10 mg/mL. If necessary, may be reconstituted with a minimum of 2 mL to a final concentration of 100 mg/mL.

Reconstituted solution for injection

Physically stable for 8 hours at normal room temperature and light or up to 72 hours at 4°C. When protected from light, solutions are stable for at least 24 hours at room temperature (1% decomposition) and at least 96 hours when refrigerated (<1% decomposition). However, the manufacturer states that, at 20°C, the solution is not stable for more than 8 hours. A colour change from pale yellow to pink or red is a sign of decomposition.

Diluted solution for infusion

Compatible in D5W and NS for 8 hours at room temperature and 24 hours at 4°C. Trissel indicates stability of 24 hours at room temperature and at 4°C when protected from light, with 5% decomposition in 24 hours if solutions were not protected from light. Another study cited by Trissel indicates that less than 10% decomposition occurred when a 1.7 g/L solution in D5W was stored in glass and PVC containers at room temperature for 24 hours.

Compatible with ondansetron. It is recommended that dacarbazine not be mixed with other drugs.

Incompatible (immediate pink precipitate) with hydrocortisone sodium succinate; no precipitate was noted with hydrocortisone phosphate. Some combinations with heparin have also been reported to be incompatible, with immediate precipitation possible.

DOSE ADJUSTMENT CRITERIA

Renal failure: *(Suggested action)*
Consider dose reduction if renal function is reduced (eg. reduced creatinine clearance/serum creatinine)

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status- Intermediate Level	
CDHA Status	Formulary
Pharmacare Status	Non-Formulary

DACTINOMYCIN

(Antineoplastic Agent; Antibiotic)

Revision Date: Feb 03

DRUG

COMMERCIAL PRODUCT DESCRIPTION

Brand Name Cosmegen® Vials of 500, .g (0.5mg) for reconstitution

MECHANISM OF ACTION

Binds to the guanine portion of DNA, intercalating between guanine and cytosine base pairs, inhibiting DNA and RNA synthesis and protein synthesis.

PHARMACOKINETICS

Oral Absorption

poorly absorbed from gastrointestinal tract

Distribution

rapid entry into nucleated cells (bone marrow > plasma), crosses placenta, excretion in breast-milk unknown cross blood brain barrier?

poor penetration into CSF

Vd no information PPB 5%

Metabolism

Minimal, 15% eliminated by hepatic metabolism

metabolite(s) active- no inactive- yes

Excretion

15% as intact drug in feces in 1 week, in urine, in bile (50%)

urine 15% as intact drug in 1 week

t½ 36 hours; prolonged with hepatic dysfunction CI no information

IV COMPATIBILITY

normal saline, dextrose 5%

ROUTES

direct IV (preferred)
intermittent IV (over 10-15 minutes)

ADMINISTRATION

- Slow push through sidearm of free flowing IV (5% Dextrose or Normal Saline) over 1-5 minutes (administering nurse should be certified to administer IV push chemotherapy agents and other vesicant agents)
- Do **not** use an in-line filter
- May be mixed in 50mL minibag (5% Dextrose or Normal Saline); Infuse over 10-15 minutes
- Protect from light

DOSING

Direct intravenous:

- q2w: 1.25 mg/m²
- q3-4w: 0.75-2 mg/m² (25-50 mcg/kg)
- q3-4w: 0.5mg daily for 5 days
- q4-6w: 400-600 mcg/m²/day (10-15 mcg/kg/day) x 5 days

Isolated perfusion:

- q3-4w: upper extremity: 35mcg/kg
- lower extremity or pelvis: 50 mcg/kg

Dosage calculation in obese or edematous patients should be based on body surface area in efforts to relate the dose to lean body mass.

Pediatric

Direct intravenous:

- q5-8w: 15 mcg/kg/day x 5 days. Maximum single dose 500 mcg.
- q3w: 45 mcg/kg. Maximum single dose 500 mcg.

Other dosing may be indicated

EXTRAVASATION HAZARD

VESICANT

(tissue damage on extravasation)

Management- stop IV, aspirate, elevate limb, cold intermittent compresses

Follow Extravasation Guidelines

SIGNIFICANT INTERACTIONS

*halogenated inhalation anesthetics (eg, enflurane, halothane), radiation therapy, vincristine

ANTIEMETIC RISK

HIGH RISK (30-90% of patients)

- Use a serotonin receptor antagonist PLUS dexamethasone pre-chemotherapy and post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

DACTINOMYCIN

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)

- * anaphylaxis (rare)
- vein irritation (pain, phlebitis)
- nausea and vomiting** (onset 1-6 hours, duration 4-20 hours)
- loss of appetite (anorexia)
- allergic (fever, chills)
- flushing of face, torso
- low calcium levels (rare, hypocalcemia)
- radiation recall reaction (rare)

EARLY ONSET (days to weeks)

- * **low WBC, RBC, platelets** (**myelosuppression**, nadir 14-21 days, recovery 21-25 days)
- mouth sores** (stomatitis, 30%)
- hair loss (rare, mild-moderate, alopecia)
- diarrhea** (30%)
- skin problems (rare, folliculitis of face and torso)
- liver problems (elevated liver function tests, ascites, liver enlargement)

DELAYED/LATE ONSET

- * cancer (rare)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth

SUGGESTED CRITERIA

- Periodic **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- Baseline **renal function tests** (if failure suspected) [serum creatinine, electrolytes & BUN]
- Local Site Toxicity ratings, if incident of phlebitis

Local Site Toxicity

0. None

1. Pain

2. Pain & inflammation; phlebitis

3. Ulceration

4. Plastic surgery

Upon Patient

Complaint Or

Clinical Event

INDICATIONS AND OTHER USES

- Ewing's sarcoma
- Rhabdomyosarcoma
- Testicular cancer
- Uterine cancer
- Wilm's tumour

OTHER ONCOLOGY USES

Germ cell tumours

Kaposi's sarcoma

Melanoma

Optic nerve glioma

Osteogenic sarcoma

CONTRAINDICATIONS

- known hypersensitivity to dactinomycin
- pregnancy and breast feeding
- low WBC, RBC, platelets (**myelosuppression**)
- infection with chicken pox or herpes zoster
- avoid in children < 6 months of age

DOSE ADJUSTMENT CRITERIA

Hepatic failure; (*Suggested action*)

Consider dose reduction if LFTs elevated (eg. Bilirubin or AST)

Continued Next Page...

DACTINOMYCIN

PHARMACEUTICAL CONSIDERATIONS

Injection

0.5 mg (500 mcg) vial; also contains 20 mg mannitol per vial; store at room temperature; protect from light.

Reconstitute powder with 1.1 mL preservative-free SWI, D5W or NS to a final concentration of 0.5 mg/mL (ie. 500 mcg/mL). Diluents containing preservatives may cause precipitation of dactinomycin.

Reconstituted solution for injection

Clear, gold-coloured solution. Chemically stable at room temperature for 2-5 months, but due to possibility of microbial contamination of the preservative-free solution, unused solutions should be discarded.

Diluted solution for infusion

Compatible with D5W and NS. Less than 10% dactinomycin loss was observed when a 9.8 mg/L D5W solution in glass or PVC containers was stored at room temperature for 24 hours.

Filtration of IV solution through cellulose acetate/nitrate ester filters (eg, Millex OR) has been reported to result in considerable loss of dactinomycin.

Polytetrafluoroethylene (eg, Millex GV) filters may bind 50-60% of dactinomycin. Polycarbonate filters bind only 0.3% and stainless steel filters bind insignificant amounts of dactinomycin.

Compatible with ondansetron. It is recommended that dactinomycin not be mixed with other drugs.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Intermediate Level

CDHA Status Formulary

Pharmacare Status Formulary (red)



DAUNORUBICIN

(Antineoplastic Agent; Anthracycline; Antibiotic)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Cerubidine®
sterile water for injection- red solution

Vials of 20mg for reconstitution with 4mL of

MECHANISM OF ACTION

Inhibition of DNA and RNA synthesis by intercalating between DNA base pairs and by steric obstruction. It intercalates at points of local uncoiling of the double helix. The exact mechanism is unclear, but it appears that direct binding to DNA (intercalation) and inhibition of DNA repair (topoisomerase 2 inhibition) result in blockade of DNA and RNA synthesis and fragmentation of DNA.

PHARMACOKINETICS

Oral Absorption

no

Distribution

Rapid and wide distribution. Highest levels in liver, kidneys, lungs, spleen, heart and small intestines. Crosses placenta. Excretion in breast-milk unknown

cross blood brain barrier? no

Vd 40 L/kg PPB 50-60%

Metabolism

liver and other tissues

metabolite(s) active- daunorubicinol

(major metabolite) inactive- yes:

aglycons, conjugates sulfates, glucuronides

Excretion

hepatobiliary secretion in feces is predominant route of elimination (40%)

urine 25% as metabolites and

unchanged drug

t_{1/2α} 45-180 minutes t_{1/2 β} 20-30 hours;

DOSING

Induction:

- usually used for induction, not for maintenance
- daily: 1-2 mg/kg (30-60 mg/m²) per day IV x 3-12 days
- total treatment course: 3-22.5 mg/kg (90-675 mg/m²) IV
- q1w: 1 mg/kg (30 mg/m²) IV
- q3-4w: 30-45 mg/m²/day IV x 3 days

Maximum lifetime dose:

- 550 mg/m² (normal cardiac function)
- 400-450 mg/m² (in combination with thoracic radiation or prior anthracycline therapy)
- Careful cardiac monitoring is important, as cardiotoxicity may occasionally occur at lower cumulative doses. If tumour responding when lifetime dose is reached, obtain cardiac consultation before continuing treatment.

Pediatric

- 60 mg/m²/day IV x 2 days
- q1w: 25 mg/m² IV x 4 weeks
- q3w: 20 mg/m²/day IV x 4 days q10d x 2 courses, then q3w
- Children less than 2 years old or <0.5 m², calculate dose based on body weight rather than body surface area (mg/kg dose can be approximated by dividing the mg/m² dose by 30).

Maximum lifetime dose:

- 500 mg/m² (normal cardiac function)
- 450 mg/m² (cardiac radiation or cardiac abnormalities)

Other dosing may be indicated in specific regimens

IV COMPATIBILITY

normal saline, dextrose 5%, lactated Ringer's

ROUTES

direct IV (preferred)
intermittent IV (over 30-60 minutes)

Continued Next Page...

DAUNORUBICIN

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)

- * anaphylaxis (rare)
- pain at injection site during injection
- facial flushing
- flare reaction (histamine release)
- nausea and vomiting** (85%)
- urine discolouration** (reddish, lasts 1-2 days)
- radiation recall reaction (rare)
- allergic (skin rash, fever)
- irregular heartbeat (uncommon, acute arrhythmias)
- increased uric acid levels (hyperuricemia)

EARLY ONSET (days to weeks)

- * **low WBC, RBC, platelets** (**myelosuppression**, nadir 6-13 days, recovery 21-24 days)
- mouth sores** (stomatitis)
- hair loss** (alopecia)
- diarrhea
- darkening of skin (hyperpigmentation)
- nail changes (including hyperpigmentation)

DELAYED/LATE ONSET (weeks- years)

- * heart problems (congestive heart failure, cardiomyopathy)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Clinical exam for symptoms of **Congestive Heart Failure**
- Periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels
- Baseline **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]

SUGGESTED CRITERIA

- Baseline **cardiac function tests** (Echo RNA and/or MUGA scans) for all patients with cardiac risk factors
- Baseline **renal function tests** (if failure suspected) [serum creatinine, electrolytes & BUN]

Cardiac

0. None

1. —

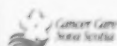
2. Asymptomatic, resting ejection fraction decline by >10% baseline; or abnormal cardiac function tests (LVEF >50) with no baseline for comparison
3. Mild Congestive Heart Failure, responds to therapy
4. Severe/refractory Congestive Heart Failure

At cumulative dose threshold and subsequent intervals

For Cardiac Toxicity Ratings:

First rating at the Daunorubicin cumulative dose **threshold of 600mg/m²**, & repeat ratings at each cumulative dose **increment of 100mg/m²** above threshold (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation)

Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.



DAUNORUBICIN

INDICATIONS AND OTHER USES

- Acute lymphocytic leukemia
- Acute non-lymphocytic leukemia
- Chronic myelogenous leukemia
- Ewing's sarcoma
- Wilms' tumour

OTHER ONCOLOGY USES

Hodgkin's disease

Lymphosarcoma

Non-Hodgkin's lymphoma

Reticulosarcoma

Rhabdomyosarcoma

CONTRAINDICATIONS

- known hypersensitivity to daunorubicin
- > maximum lifetime dose of an anthracycline (daunorubicin, doxorubicin, epirubicin, idarubicin, mitoxantrone)
- pregnancy and breast feeding
- low WBC, RBC, platelets (myelosuppression)
- heart (cardiac) failure

ANTIEMETIC RISK

HIGH RISK (30-90% of patients)

- Use a serotonin receptor antagonist PLUS dexamethasone pre-chemotherapy and post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

SIGNIFICANT INTERACTIONS

acyclovir, allopurinol, blood dyscrasia-causing medications, bone marrow depressants, colchicine, cyclosporin, hepatotoxic medications, probenecid, radiation therapy, sulfapyrazone, verapamil

ADMINISTRATIVE INFORMATION

- Slow push through sidearm of free flowing IV (5% Dextrose, Normal Saline) over 1-5 minutes (*administering nurse should be certified to administer IV push chemotherapy agents and other vesicant agents*)
- May be mixed in 50mL minibag (5% Dextrose, Normal Saline). Infuse through sidearm of free flowing IV over 10-15 minutes
- Slow down injection rate if erythematous streaking occurs
- May be infused through central venous catheter

EXTRAVASATION HAZARD

VESICANT (tissue damage on extravasation)

Management- stop IV, aspirate, elevate limb, cold intermittent compresses

Follow Extravasation Guidelines

DOSE ADJUSTMENT CRITERIA

Hepatic dysfunction

75% if Bili=26-51µmol/L or AST =60-180IU/L;

50% if Bili= 52-85µmol/L or AST>180IU/L;

Omit if Bili >85µmol/L

Renal failure

50% if Serum Creatinine >265µmol/L

(Suggested action)

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Intermediate Level

CDHA Status Formulary

Pharmacare Status Formulary (red)

DAUNORUBICIN**PHARMACEUTICAL CONSIDERATIONS****Injection**

20 mg vial; store at room temperature

Reconstitute powder with 4 mL SWI to a final concentration of 5 mg/mL

Reconstituted solution for injection

Clear, red solution. Stable 24 hours at room temperature and 48 hours when refrigerated. King states that solution is stable 7 days at room temperature. A colour change from red to blue-purple indicates decomposition; such solutions should be discarded. Contact between daunorubicin and aluminum resulted in darkening of the solution and formation of black patches on the aluminum surface after 12-24 hours. Daunorubicin should not be stored in contact with aluminum but it may be injected safely through an aluminum-hubbed needle.

Diluted solution for infusion

Stable at concentrations of 20-100 mg/L in NS, D5W, dextrose-saline combinations, or lactated Ringer's for at least 4 weeks at room temperature, protected from light. The liposomal formulation must be further diluted with D5W to a final concentration of 0.2-1 mg/mL. It should not be diluted with saline, bacteriostatic agents or any other solution and must be administered within 6 hours of dilution.

Filtration through cellulose acetate/nitrate (Millex OR) or polytetrafluoroethylene (Millex FG) filters results in only slight binding of daunorubicin. It is recommended by the manufacturer that the liposomal form not be filtered during administration but, if a filter is used, it should be of a pore size not less than 5 microns.

Compatible with ondansetron. Some mixtures with hydrocortisone, cytarabine and etoposide are compatible. It is recommended that daunorubicin not be mixed with other drugs. Incompatible with dexamethasone and heparin.



DEXAMETHASONE

(Antiemetic, Anti-inflammatory Agent, Corticosteroid)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Decadron® Vials with 4mg/mL & 10mg/mL
 White pentagonal tablets with 0.5mg & 4mg
 Dexasone® Oval yellow tablets with 0.5mg, oval pale blue tablets with 0.75%, oval green tablets with 4mg

Generic products available

MECHANISM OF ACTION

The mechanism of antiemetic activity is unknown. It decreases inflammation by suppression of migration of polymorphonuclear leucocytes and reversal of increased capillary permeability, suppresses normal immune response.

PHARMACOKINETICS

Oral Absorption

rapidly and almost completely

Distribution

rapidly removed from the blood and distributed to muscles, liver, skin, intestines, kidneys, excretion in breast-milk- unknown cross blood brain barrier? No information (crosses placenta)

Vd- No information PPB- yes

Metabolism

primarily rapid hepatic, renal and tissue; mediated by Cytochrome P450 enzyme CYP 3A4

metabolite(s) inactive- yes

Excretion

primarily by renal excretion of inactive metabolites

t½ normal renal function: 1.8-3.5 hours; biological t½: 36-54 hours

IV COMPATIBILITY

sodium chloride 0.9%, dextrose 5% compatible with blood for transfusion

ROUTES

oral
 parenteral
 dexamethasone- IM or IV injection

ADMINISTRATION

- Doses ≤ 10mg may be given as direct IV push or through side arm of a free-flowing IV, over 5 to 10 minutes, followed by a flush with Normal Saline (administering nurse should be certified to administer IV push chemotherapy agents and other vesicant agents)
- May be mixed in 50mL minibag (5% Dextrose, Normal Saline); Give over 10-30 minutes
- May be admixed with Metoclopramide or Ondansetron in same minibag

DOSING

Oral:

- 4-8 mg po before chemotherapy, and q24h after chemotherapy (as antiemetic)
- May increase pre-chemotherapy dose up to 20mg po (dose-response relationship)
- 20mg po 12 hours and 6 hours before paclitaxel (prevention of hypersensitivity)
- 8mg po bid for 3 days before docetaxel (prevention of hypersensitivity & fluid retention)

Other dosing may be indicated in specific regimens

- 40mg po daily with doxorubicin and vincristine (multiple myeloma)
 - Many other doses and combinations used in oncology
 - Take tablets with food, if possible, do not take at bedtime (qhs specified in some regimens)
- Injection:
- 8-20mg IV before chemotherapy (with serotonin receptor antagonist as antiemetic, for highly emetogenic chemotherapy)
 - Do not give for antiemesis if a steroid is included in the treatment regimen

Continued Next Page...

DEXAMETHASONE

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

- * allergic reactions (rare)
- sudden blindness
- pain or tingling at injection site***
- gastrointestinal irritation***

EARLY ONSET (days to weeks)

- diabetes mellitus***
- acne or other skin problems
- cataracts
- immunosuppression

DELAYED/LATE ONSET (weeks to years)

- Cushing's syndrome
- osteoporosis
- edema

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Serum glucose levels (for diabetic patients on multiple day treatments) and serum electrolyte levels
- Clinical exam for proximal muscle myopathy

SUGGESTED CRITERIA

- Baseline ophthalmological exam for evidence of cataracts
- Full assessment by ophthalmologist if cataracts suspected
- Periodic tests for hemoglobin, fecal occult blood if abdominal bleeding suspected
- Periodic blood tests for electrolytes, especially potassium

INDICATIONS AND OTHER USES

- Leukemias & lymphomas, palliative management
- Acute leukemia of childhood
- Cerebral edema (brain tumours or metastases)
- Idiopathic thrombocytic purpura & secondary thrombocytopenias
- Multiple non-oncology indications
- Management of nausea & vomiting associated with chemotherapy or radiotherapy

OTHER ONCOLOGY USES

Prevention of hypersensitivity reaction with taxane chemotherapy agents

SIGNIFICANT INTERACTIONS

NSAIDs, ASA, aminoglutethimide, amphotericin B, carbonic anhydrase inhibitors, antidiabetic agents, diuretics, hepatic-enzyme-inducing agents, mitotane, estrogens, isoniazid, immunosuppressants
Cytochrome P450 Inhibitor

EXTRAVASATION HAZARD

may produce atrophy at injection site; rotate sites for repeated injections

CONTRAINDICATIONS

- arthroplasty of joints
- thromboembolic disorders
- osteoporosis (juxta-articular, non-arthritis)

PHARMACEUTICAL CONSIDERATIONS

Tablets, 0.5mg, 0.75mg and 4 mg tablets (various generic brands)

Injection

Infuse over 5 to 15 minutes just prior to chemotherapy administration; do not give by IV push

May be admixed with ondansetron in 50mL D5W; stable for 2 days on storage at room temperature or 7 days on storage under refrigeration.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-

Injection-Basic Level;

Oral- Take Home Prescription

CDHA Status Formulary

Pharmacare Status Formulary

DEXRAZOXANE

(Cardioprotective Agent)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Zinecard® **Vials with 250mg & 500mg Dextrazoxane, for reconstitution with 25mL or 50mL of M/6 sodium lactate diluent (included)**

MECHANISM OF ACTION

Dextrazoxane is an EDTA-analog. It is hydrolyzed intracellularly to ICRF-198, a heavy metal chelator. Intracellular binding to iron inhibits doxorubicin generation of oxygen free radicals, thought to be responsible for the cardiac toxicity.

PHARMACOKINETICS

Oral Absorption

no information

Distribution

cross blood brain barrier? no information

Vd 0.8-2.1 L/kg

PPB not bound to plasma proteins

Metabolism

metabolized to: a diacid-diamide cleavage product, two monoacid-monoamide ring products

Excretion

renal 48%

t_{1/2α}: 0.5-1.5 hours t_{1/2β}: 2.0-5.1 hours

IV COMPATIBILITY

sodium chloride 0.9%

Dextrose 5%

sodium lactate

ROUTES

intravenous slow infusion or rapid injection (5 to 15 minutes)

ADMINISTRATION

- Transfer total volume of reconstituted solution to empty minibag. Infuse over 10-15 minutes
- Slow push through sidearm of free flowing IV (5% Dextrose, Normal Saline) (administering nurse should be certified to administer IV push chemotherapy agents)
- Give anthracycline dose within 15-30 minutes after the starting time for Dextrazoxane

EXTRAVASATION HAZARD

none

DOSING

Injection:

- 500mg/m² IV as a slow IV push or rapid IV infusion (from a bag with undiluted solution) in the period of 30 minutes to 15 minutes prior to doxorubicin injection
- Dose may be calculated at 10:1 ratio with doxorubicin (e.g. 250mg/m² dextrazoxane: 25mg/m² doxorubicin)

Pediatric: Safety & effectiveness not established

Other dosing may be indicated

CONTRAINDICATIONS

- pregnancy

INDICATIONS AND OTHER USES

- Reduction or prevention of cardiac toxicity from doxorubicin (and other anthracyclines). Used for treatment of breast cancer in which previous treatment included an anthracycline at a cumulative dose of 300 mg/m² of doxorubicin or 600 mg/m² of epirubicin and for which further disease response may be achieved with anthracycline-based therapy

OTHER ONCOLOGY USES

Reduction or prevention of cardiac toxicity from doxorubicin, used for treatment of pediatric malignancies

DEXRAZOXANE

SIDE EFFECTS

* may be life-threatening

side effects in **bold**, *italic* type are common

IMMEDIATE ONSET (hours to days)

pain at injection site, phlebitis
stomatitis, myelosuppression

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment

SUGGESTED CRITERIA

- Monitor **liver function tests** (if liver failure suspected) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]
- Monitor **cardiac function tests** (Echo, RNA and/or MUGA scans) for all patients with cardiac risk factors

PHARMACEUTICAL CONSIDERATIONS

Injection

Single dose vials with 250mg or 500mg dexrazoxane. Injection kits include 25mL or 50mL vials of M/6 sodium lactate solution for reconstitution of dexrazoxane. Store at room temperature.

Reconstitute vial with M/6 sodium lactate solution (250mg powder dissolved in 25mL, 500mg powder dissolved in 50mL) to a final concentration of 10mg/mL. Store in refrigerator at 2-8 °C after reconstitution.

May administer as slow IV push, or may transfer solution to empty IV bag and administer by rapid drip IV infusion. Discard unused solutions.

Dexrazoxane is considered incompatible with other solutions.

SIGNIFICANT INTERACTIONS

none reported in the literature
doxorubicin should be administered
AFTER dexrazoxane

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-

Intermediate Level; *Indication*

restriction- Provincial Cancer Drug Formulary

CDHA Status

Formulary- Restricted; Dexrazoxane

Request Form required

Pharmacare Status Non-Formulary



DOCETAXEL

(Antineoplastic Agent; Antimicrotubular)

Revision Date, Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Taxotere® Vials with 20mg/0.5mL & 80mg/2mL for dilution into infusate solution (non-PVC bags and tubing)

MECHANISM OF ACTION

Docetaxel is a taxane derivative similar to paclitaxel. It promotes microtubule assembly and inhibits microtubule disassembly; stabilizing microtubules. This results in inhibition of DNA, RNA, and protein synthesis. Most activity occurs during the M phase of the cell cycle.

PHARMACOKINETICS

Oral Absorption

No information

Distribution

No information; excretion in breast-milk unknown

cross blood brain barrier? No information
Vd- 80-90 L/m² PPB- very high (97%)

Metabolism

hepatic; extensively by Cyt P450 subfamily 3A; one major and three minor metabolites

Excretion

about 75% is eliminated in the feces;
about 5% is found in the urine
urine yes (5%)

Cl 21L/hr/m²

t_{1/2} Dose-dependent; >70mg/m²-
triphasic elimination profile

t_{1/2α} 4 min (distribution), t_{1/2β} 36 min,

t_{1/2γ} 11.1 hrs

IV COMPATIBILITY

sodium chloride 0.9% Dextrose 5%

ROUTES

intravenous infusion over 1 hour

ADMINISTRATION

- ALWAYS premedicate with Dexamethasone; May give H1 blocker (e.g. Diphenhydramine) and/or H2 blocker (e.g. Ranitidine) IV 30 minutes before dose
- Mix in 250-500mL polyolefin bag or glass bottle (5% Dextrose or Normal Saline) to a maximum concentration of 0.3-0.9mg/mL; Use non-PVC equipment; Infuse through main IV line over 1-2 hour(s)
- Infusions may be given over a longer period (ie. begin at 60 mL/h and titrate the rate upwards in increments of 10 mL/h to a maximum of 250 mL/h) to decrease the incidence of hypersensitivity reactions.

EXTRAVASATION HAZARD

may be an IRRITANT

local reactions at the injection site (3-4%)

SIGNIFICANT INTERACTIONS

bone marrow depressants, radiation therapy

enzyme inhibitors of CYT P450 3A, immunosuppressants, other antineoplastic agents

Cytochrome P450 3A Substrate

ANTIEMETIC RISK

INTERMEDIATE RISK (10-30% of patients)

- Use a dexamethasone pre-chemotherapy and a dopamine receptor antagonist PRN post-chemotherapy

INDICATIONS AND OTHER USES

- Lung cancer, non-small cell
- Ovarian cancer
- Breast Cancer

OTHER ONCOLOGY USES

Breast cancer

Head and neck cancer

Lung cancer, small cell

Mesothelioma

Prostate cancer

Urothelial transitional cell cancer

CONTRAINDICATIONS

- hepatic function impairment
- bone marrow depressants

Continued Next Page...

DOCETAXEL

DOSING

3 weeks:

- 100 mg/m² (range 40-100 mg/m²) IV for one dose on day 1

3 weeks:

- 20-40 mg/m² IV for one dose on days 1 and 8 (total dose per cycle 40-80 mg/m²)⁵

4 weeks:

- 25-90 mg/m² IV for one dose on day 1

8 weeks:

- 36 mg/m² IV for one dose on days 1, 8, 15, 22, 29 and 36 (total dose per cycle 216 mg/m²)
- NB, sometimes referred to as the "weekly schedule"

Premedication regimen:

3 weeks:

- dexamethasone 8 mg PO twice a day for 3 consecutive days starting one day prior to each docetaxel infusion (total dose per cycle 48 mg) **Note:** Pre- and Post-chemotherapy dexamethasone equals a total of 6 doses or 3 days.
- Alternate premedication: dexamethasone 8 mg PO the night before treatment, the morning of treatment and one hour before treatment.)
- antihistamines have not been shown to be useful in controlling fluid retention

8 weeks:

- dexamethasone 8 mg PO twice a day for 3 doses starting the night before, morning of and evening after treatment (total dose per cycle 24 mg)
- *Concurrent radiation:*

1 week:

- investigational, 20 mg/m² IV for one dose on day 1

High dose chemotherapy with peripheral blood stem cell support:

- 100 mg/m² IV for one dose on day 2

Other dosing may be indicated in specific regimens

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

The incidence of adverse effects may increase with impaired hepatic function

IMMEDIATE ONSET (hours to days)

hypersensitivity reactions (Symptoms- mild (flushing, rash, chest tightness, back pain, drug fever and chills) to severe (hypotension, bronchospasm and generalized rash and erythema)- Usually with the first or second dose, may occur within a few minutes of starting the infusion

nausea/vomiting (40%)

neurosensory effects (49%)

DELAYED/LATE ONSET

weight gain

EARLY ONSET (days to weeks)

* **myelosuppression**

* **stomatitis** (50%)

alopecia (80%)

myalgia (20%)

hypotension

edema



DOCETAXEL

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Baseline liver function tests** (if liver failure suspected) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- Watch for symptoms of **fever or infection**
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Skin assessment** at each visit, including nails
- Monitor fluid retention at each visit

Skin Toxicity

- 0. None
- 1. Hyperpigmentation
- 2. Atrophy
- 3. Subcutaneous fibrosis
- 4. Desquamation, ulceration or necrosis

Fluid Retention

- 0. None
- 1. Mild peripheral edema
- 2. Pleural effusion, outpatient management
- 3. Pleural effusion, inpatient
- 4. Intubation required

Rated At Each Clinic Visit

SUGGESTED CRITERIA

Neurologic (Sensory) and hypersensitivity toxicity ratings at visit if patient complains of symptoms

Baseline & periodic **vital signs**
Sensory

- 0. No change
 - 1. Mild paraesthesia; no deep tendon reflex
 - 2. Mild/moderate sensory loss; moderate paraesthesia
 - 3. Sensory loss interferes with function
- #### Hypersensitivity/Allergy
- 0. None
 - 1. Transient rash, fever $<38^{\circ}\text{C}$
 - 2. Urticaria, fever $\geq 38^{\circ}\text{C}$, mild bronchospasm
 - 3. Serum sickness, bronchospasm, requires parenteral meds
 - 4. Anaphylaxis

Rated In Response To Patient Complaint

DOSE ADJUSTMENT CRITERIA

Hepatic dysfunction

- 1. If AST or ALT $>60\text{IU/L}$ ($>1.5\text{X ULN}$) or if Alk Phos $>300\text{IU/L}$ ($>2.5\text{X ULN}$), **REDUCE** to 75%
- 2. If AST or ALT $>200\text{IU/L}$ ($>3.5\text{X ULN}$) or if Alk Phos $>720\text{IU/L}$ ($>6\text{X ULN}$), **HOLD** dose and contact physician

ALTERNATE ADJUSTMENT:

- 3. If LFTs $>1.5\text{x ULN}$ or Bilirubin $>\text{ULN}$ ($>26\mu\text{mol/L}$) during treatment, **HOLD** dose for 3 weeks and re-test
- ULN = upper limit of normal for lab value
(Recommended action)

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Intermediate Level: *Indication restriction-* Provincial Cancer Drug Formulary

CDHA Status
Formulary-Restricted Status
Pharmacare Status Non-Formulary

DOCETAXEL

PHARMACEUTICAL CONSIDERATIONS

Concentrate for injection:

20 mg (0.5 mL) or 80 mg (2 mL) vials, each mL contains 40 mg docetaxel and 1040 mg polysorbate 80. Diluent 1.5 mL (for 20 mg vial) and 6 mL (for 80 mg vial) contains ethanol 95%. Store under refrigeration. Protect from bright light (eg, retain in original package). Freezing does not adversely affect the product.

Reconstitution:

Allow vials to stand at room temperature for approximately 5 minutes. Reconstitute concentrate with entire contents of the 1.5 mL diluent vial (for 20 mg vial); and with entire contents of the 6 mL diluent vial (for 80 mg vial) to give 10 mg/mL solution. Gently rotate for approximately 15 seconds to assure full mixture of the concentrate and diluent. Contact of the concentrate with plasticized polyvinyl chloride (PVC) equipment or devices used to prepare solution for infusion is not recommended. The vials contain overfills of docetaxel and diluent to allow for loss due to foaming, adhesion to vial walls, and dead space during initial dilution of the concentrate.

Reconstituted solution for injection:

The docetaxel premix solution (10 mg/mL) should be clear; however, there may be some foam on top of the solution due to the polysorbate 80. Allow the premix solution to stand for a few minutes to allow foam to dissipate. It is not required that all foam dissipate prior to continuing the preparation process. Stable for 8 hours at room temperature or under refrigeration.

Diluted solution for infusion:

To minimize patient exposure to plasticizer DEHP (di-2-ethylhexyl phthalate), which may be leached from PVC infusion bags or sets, docetaxel infusion solution should be stored in bottles (glass, polypropylene) or plastic bags (polypropylene, polyolefin) and administered through polyethylene-lined administration sets. Dilute with NS or D5W to produce a final concentration of 0.1-0.9 mg/mL. If a dose greater than 200 mg is required, use a larger volume of the infusion vehicle so that a concentration of 0.74 mg/mL is not exceeded. Stable in NS or D5W for 8 hours at room temperature or under refrigeration. Administer under ambient lighting conditions. In-line filters must be avoided.

Bacterial Challenge:

Docetaxel 0.8 mg/mL diluted in NS did not exhibit an antimicrobial effect on the growth of four organisms inoculated into the solution. Diluted solutions should be stored under refrigeration whenever possible, and the potential for microbiological growth should be considered when assigning expiration periods.

Compatibility:

The following are compatible via Y-site injection: amifostine, butorphanol, calcium gluconate, chlorpromazine, dexamethasone, diphenhydramine, droperidol, famotidine, gemcitabine, granisetron, haloperidol, heparin, hydrocortisone, hydromorphone, hydroxyzine, leucovorin, lorazepam, magnesium sulfate, meperidine, mesna, metoclopramide, morphine, ondansetron, potassium chloride, prochlorperazine, promethazine, ranitidine and sodium bicarbonate.

Incompatibility: The following are incompatible via Y-site injection: doxorubicin HCl liposome, methylprednisolone sodium succinate and nalbuphine.



DOXORUBICIN

(Antineoplastic Agent; Anthracycline; Antibiotic)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Adriamycin® Vials with 10mg/5mL, 50mg/25mL, 200mg/100mL
 Generic products available Vials with 10mg, 50mg, 150mg for reconstitution

MECHANISM OF ACTION

Inhibition of DNA and RNA synthesis by intercalation between DNA base pairs and by steric obstruction. It intercalates at points of local uncoiling of the double helix. The exact mechanism is unclear, it appears that direct binding to DNA (intercalation) and inhibition of DNA repair (topoisomerase 2 inhibition) result in blockade of DNA and RNA synthesis and fragmentation of DNA. Doxorubicin is also a powerful iron chelator; the iron-doxorubicin complex can bind DNA and cell membranes and produce free radicals that immediately cleave the DNA and cell membranes.

PHARMACOKINETICS

Oral Absorption

poor (~50%)

Distribution

highest concentrations in liver, spleen, kidney, heart, small intestines, lung; crosses placenta; found in breast milk
 cross blood brain barrier? no
 Vd- 25 L/kg PPB- 70%

Metabolism

liver (major site) and other tissues; elimination primarily via liver and biliary system

metabolite(s) active- doxorubicinol (major metabolite) inactive- Yes: aglycones, conjugated sulfates, glucuronides

Excretion

predominantly in bile (80%; 50% as unchanged drug, 30% as metabolites); 40% of dose is excreted in the bile within 7 days (42% unchanged drug, 22% doxorubicinol, 36% other metabolites)
 urine 3-10% is excreted in the urine as metabolites (1% doxorubicinol, 1% adrimycine aglycones) and unchanged drug.

Distribution $t_{1/2} \alpha$ 10 minutes

Elimination $t_{1/2} \beta$ 1-3 hours for doxorubicin; 3-3.5 hours for metabolites

Terminal $t_{1/2} \gamma$ 29.6 hours (17-30 hours)

Cl- Male: 113 L/hour; Female: 44 L/hour

IV COMPATIBILITY

normal saline, dextrose 5%, lactated Ringer's

ROUTES

direct IV (preferred)
 intermittent IV
 (in 100 mL over 1 h, venous access device preferred)
 continuous IV (via venous access device)
 intravesical (2 mg/mL in Normal Saline)

ADMINISTRATION

- Slow push through sidearm of free flowing IV (5% Dextrose, Normal Saline) over at least 3-5 minutes (administering nurse should be certified to administer IV push chemotherapy agents and other vesicant agents)
- Slow down injection rate if erythematous streaking occurs
- May be administered by continuous infusion using ambulatory infusion pump; Infuse through central venous access device; do not filter
- Protect from light

ANTIEMETIC RISK

HIGH RISK (30-90% of patients)
 • Use a serotonin receptor antagonist PLUS dexamethasone pre-chemotherapy and post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

Continued Next Page...

DOXORUBICIN

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

- * anaphylaxis (rare)
- flare reaction (histamine release)
- pain at injection site during injection
- vein irritation (phlebitis)
- facial flushing, nasal congestion
- nausea and vomiting** (60%, onset 3-4 hours, duration 6-12 hours)
- diarrhea
- urine discolouration** (reddish, lasts 1-2 days)
- radiation recall reaction (rare)
- irregular heartbeat** (41%, acute transient arrhythmias)
- increased uric acid levels (hyperuricemia)

EARLY ONSET (days to weeks)

- * **low WBC, RBC, platelets** (**myelosuppression** nadir 6-13 days, recovery 21-24 days)
- mouth sores** (stomatitis starts in 5-10 days)
- diarrhea
- allergic (skin rash, fever, chills)
- eye irritation (rare, conjunctivitis)
- hair loss** (90%, alopecia)

DELAYED/LATE ONSET (weeks - years)

- * heart problems (congestive heart failure and/or cardiomyopathy, dose-related)
- darkening of skin (hyperpigmentation)
- nail changes
- infertility**

DOSING

Intravenous:

- q1-2w: 10-30 mg/m² bolus
- q3-4w: 60-90 mg/m² bolus
- q3-4w: 20-30 mg/m²/day bolus for 3 consecutive days
- q3w: 60-75 mg/m² 10 hour infusion
- q3-4w: 60-90 mg/m² 24-96 hour infusion

Intra-arterial:

- q3-4w: 25 mg/m²/day for 3 consecutive days

Intravesical:

- q1w: 50-80 mg via bladder instillation, retained 1-2 hours, weekly x 4 then monthly

Maximum lifetime dose:

- 450 mg/m² (normal cardiac function)
- 300 mg/m² (in combination with thoracic radiation or cyclophosphamide)
- Careful cardiac monitoring is important, as cardiotoxicity may occasionally occur at lower cumulative doses. If tumour responding when lifetime dose reached, obtain cardiac consultation before continuing treatment.

Pediatric

Intravenous:

- 45-75 mg/m² q3-8w IV
- 20-30 mg/m²/day IV x 3 days

Other dosing may be indicated in specific regimens

DOSE ADJUSTMENT CRITERIA

Hepatic dysfunction

1. If Bili = 26- 51 µmol/L or AST = 60-180 IU/L, **REDUCE to 50%** dose
2. If Bili = 52- 85 µmol/L or AST > 180 IU/L, **REDUCE to 25%** dose
3. If Bili > 85µmol/L, **OMIT** dose

Renal failure (Suggested action)

1. If Serum Creatinine > 265 µmol/L, **REDUCE to 50%** dose

CONTRAINDICATIONS

- pregnancy and breast feeding
- low WBC, RBC, platelets (myelosuppression)
- > maximum lifetime dose of an anthracycline (daunorubicin, doxorubicin, epirubicin, idarubicin, mitoxantrone)
- liver (hepatic) failure
- heart (cardiac) failure

Continued Next Page...

DOXORUBICIN

INDICATIONS AND OTHER USES

- | | |
|---|--|
| <ul style="list-style-type: none"> • Acute lymphocytic leukemia • Acute myeloblastic leukemia • Acute non-lymphocytic leukemia • Bladder cancer • Breast cancer • Endometrial cancer • Gastric cancer • Head and neck cancer, squamous cell • Hodgkin's disease • Lung cancer, small cell • Lung cancer, non-small cell • Neuroblastoma • Non-Hodgkin's lymphoma • Osteogenic sarcoma • Ovarian cancer • Sarcoma, soft tissue | <ul style="list-style-type: none"> • Testicular cancer • Thyroid cancer • Wilms' tumour <p>OTHER ONCOLOGY USES</p> <p><i>Ewing's sarcoma</i>
 <i>Kaposi's sarcoma</i>
 <i>Rhabdomyosarcoma</i>
 <i>Adrenocortical cancer</i>
 <i>Carcinoid syndrome (small bowel)</i>
 <i>Gynecological sarcoma</i>
 <i>Hepatic cancer</i>
 <i>Islet cell cancer</i>
 <i>Multiple myeloma</i>
 <i>Pancreatic cancer</i>
 <i>Prostate cancer</i>
 <i>Retinoblastoma</i></p> |
|---|--|

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- Clinical exam for symptoms of **Congestive Heart Failure**
- Periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels
- Baseline **liver function tests** (especially if poor Performance Status) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]

SUGGESTED CRITERIA

- Baseline **cardiac function tests** (Echo RNA and/or MUGA scans) for all patients with cardiac risk factors
- Local Site Toxicity ratings, if incident of phlebitis

Local Site Toxicity

0. None
1. Pain
2. Pain & inflammation; phlebitis
3. Ulceration
4. Plastic surgery

Upon Patient Complaint Or Clinical Event

Cardiac

0. None
1. —

2. Asymptomatic, resting ejection fraction decline by >10% baseline; or abnormal cardiac function tests (LVEF >50) with no baseline for comparison
3. Mild Congestive Heart Failure, responds to therapy
4. Severe/refractory Congestive Heart Failure

For Cardiac Toxicity Ratings

First rating at the Doxorubicin cumulative dose **threshold** of **300mg/m²**, & repeat ratings at each cumulative dose **increment** of **100mg/m²** above threshold (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation)

Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

At cumulative dose threshold and subsequent intervals

DOXORUBICIN

SIGNIFICANT INTERACTIONS

anticonvulsant drugs, barbiturates, cyclophosphamide, digoxin, quinolones (ciprofloxacin, norfloxacin, ofloxacin), mercaptopurine, paclitaxel, radiotherapy, streptozocin, trastuzumab, verapamil, other antineoplastic agents
Cytochrome P450 Substrate

EXTRAVASATION HAZARD

VESICANT (tissue damage on extravasation)
Management- stop IV, aspirate, elevate limb, cold intermittent compresses
Follow Extravasation Guidelines

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status- Intermediate Level
CDHA Status Formulary
Pharmacare Status Formulary (red)

PHARMACEUTICAL CONSIDERATIONS

Injection

Adriamycin RDF: Doxorubicin powder (generic) may contain methyl paraben (to enhance dissolution) 1 mg/10 mg doxorubicin and lactose 5 mg/10 mg doxorubicin. Store at room temperature, protected from sunlight (eg. store in carton until use).
Adriamycin PFS: 2 mg/mL clear, red, preservative-free solution. Also contains hydrochloric acid to adjust pH. Store in refrigerator; protect from sunlight (eg. store in carton until use). Remains stable at room temperature for 7 days, however the manufacturer recommends discarding the unused portion of vials.
Reconstitute powder with NS to a final concentration of 2 mg/mL. Do not use bacteriostatic diluents; early experience with doxorubicin suggested that the use of diluents containing benzyl alcohol resulted in hypersensitivity reactions. Vials are under negative pressure.

Reconstituted solution for injection

Clear, red solution. A colour change from red to purple indicates decomposition and such discoloured solutions should be discarded. The reconstituted solution is stable for at least 24 hours at room temperature and 48 hours under refrigeration. Walker et al reported physical stability of 124 days at 4 and 23°C when a 2 mg/mL solution was stored in its original vial. They also reported physical stability for 124 days when 1 and 2 mg/mL solutions were stored in Terumo or Monoject syringes at 4 and 23°C. Solutions should be protected from direct light. Doxorubicin should not be stored in contact with aluminum but may be safely injected through an aluminum-hubbed needle.

Diluted solution for infusion

Stable and compatible for at least 24 hours at room temperature in D5W, NS or lactated Ringer's injection. Admixture of doxorubicin (1.4 mg/mL) plus vincristine (0.033 mg/mL) in NS or sodium chloride 0.45% and dextrose 2.5% injection are stable at least 4 days in PVC containers and Pharmacia cassettes at temperatures 37°C.

Compatible with ondansetron. Some mixtures with dacarbazine, vinblastine and vincristine are reported stable for at least 24 hours. It is recommended that doxorubicin not be mixed with other drugs. Incompatible with aminophylline, cephalothin, dexamethasone, diazepam, fluorouracil, furosemide, heparin and hydrocortisone.



EPIRUBICIN

(Antineoplastic Agent; Anthracycline; Antibiotic)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Pharmorubicin® Vials with 10mg/5mL, 50mg/25mL, 200mg/100mL
Vials with 10mg, 50mg for reconstitution

MECHANISM OF ACTION

Epirubicin is an anthracycline cytotoxic agent. The precise mechanism of its cytotoxic and antiproliferative effect has not been elucidated. Epirubicin is known to inhibit DNA and RNA synthesis by steric obstruction after intercalating between DNA base pairs: active throughout entire cell cycle. Intercalation triggers DNA cleavage by topoisomerase 2, resulting in cytotoxic activity. It also inhibits DNA helicase, and generates cytotoxic free radicals.

PHARMACOKINETICS

Oral Absorption

no

Distribution

highest concentrations in liver, spleen, kidney, small intestines; excretion in breast-milk unknown

cross blood brain barrier? no information

Vd 1430 L/m² 31.8-46.1 L/kg

PPB 77% (albumin)

Metabolism

rapidly and extensively metabolized in liver and other tissues (including RBC's routes)

metabolite(s): inactive- Yes

active- epirubicinol (major metabolite)

Excretion

biliary excretion is major route of elimination (40% within 72 hours), renal urine 9-11% within 48 hours

t_{1/2} α 3-5 minutes t_{1/2} β 1.1-2.6 hours

t_{1/2} γ 30-40 hours

mean terminal: 33 hours

Cl 0.8-1.5 L/minute

IV COMPATIBILITY

normal saline, dextrose 5%

ROUTES

direct IV (preferred)

intermittent IV (in 100 mL over 1 h, VAD preferred)

ADMINISTRATION

- Slow push through sidearm of free flowing IV (5% Dextrose, Normal Saline) over at least 3-5 minutes (*administering nurse should be certified to administer IV push chemotherapy agents*)
- Slow down injection rate if erythematous streaking occurs
- Protect from light
- May administer dose in 50 mL NS or D5W and infuse over 15 minutes.

EXTRAVASATION HAZARD

VESICANT (tissue damage on extravasation)

Management: stop IV, aspirate, elevate limb, cold intermittent compresses
Follow Extravasation Guidelines

CONTRAINDICATIONS

- known hypersensitivity to epirubicin
- pregnancy and breast feeding
- low WBC, RBC, platelets (myelosuppression)
- > maximum lifetime dose of an anthracycline or anthracenedione (daunorubicin, doxorubicin, epirubicin, mitoxantrone, idarubicin)
- liver problems (hepatic failure)
- heart (cardiac) disease including unstable hypertension, angina or arrhythmias

INDICATIONS AND OTHER USES

- Breast cancer
- Gastric cancer
- Hodgkin's disease
- Lung cancer
- Non-Hodgkin's lymphoma
- Ovarian cancer

OTHER ONCOLOGY USES

Acute leukemia
Pancreatic cancer
Sarcoma, soft tissue

EPIRUBICIN

SIDE EFFECTS

* may be life-threatening

side effects in **bold**, *italic* type are common

IMMEDIATE ONSET (hours to days)

- flare reaction (histamine release- Symptoms: erythematous streaking and/or urticaria along the vein proximal to the site of administration)
- vein irritation (phlebitis)
- nausea and vomiting** (53%, 7% severe)
- urine discolouration** (reddish, lasts 1-2 days)
- irregular heartbeat (transient arrhythmias)
- radiation recall reaction (rare)

EARLY ONSET (days to weeks)

- * **low WBC, platelets (myelosuppression)**, nadir 10-14 days, recovery 21 days)
- mouth sores (11%, stomatitis)
- diarrhea
- hair loss** (54%, alopecia)
- irregular heartbeat (transient ECG changes and arrhythmias)

DELAYED/LATE ONSET (weeks to years)

- * heart problems (congestive heart failure and/or cardiomyopathy, dose-related)

DOSING

Intravenous:

- q1w: 12.5-25 mg/m² IV
- q2w: 35 mg/m² IV
- q3-4w: 50-120 mg/m² IV

Maximum lifetime dose:

- 1000 mg/m² (normal cardiac function, less in children)
- 650 mg/m² (in combination with thoracic radiation or previous anthracycline, anthracenedione or cyclophosphamide treatment)
- Careful cardiac monitoring is important, as cardiotoxicity may occasionally occur at lower cumulative doses. If tumour responding when lifetime dose reached, obtain cardiac consultation before continuing treatment.

Pediatric: Safety & effectiveness not established

Other dosing may be indicated in specific regimens

DOSE ADJUSTMENT CRITERIA

Hepatic dysfunction

- 1 If Bili = 35- 51 µmol/L or AST = 60-180 IU/L, **REDUCE** to 50% dose
- 2 If Bili = 52- 85 µmol/L or AST > 180 IU/L, **REDUCE** to 25% dose
- 3 If Bili > 85µmol/L, **OMIT** dose

Renal failure (*Suggested action*)

- 1 If Serum Creatinine > 265 µmol/L, **REDUCE** to 50% dose

ANTIEMETIC RISK

HIGH RISK (30-90% of patients)

- Use a serotonin receptor antagonist PLUS dexamethasone pre-chemotherapy and post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

SIGNIFICANT INTERACTIONS

cimetidine, other antineoplastic agents, quinine, trastuzumab, verapamil

EPIRUBICIN

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Clinical exam for symptoms of **Congestive Heart Failure**
- Periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels (especially if poor Performance Status)
- Baseline **liver function tests** (especially if poor Performance Status) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]

SUGGESTED CRITERIA

- Baseline **cardiac function tests** (Echo RNA and/or MUGA scans) for all patients with cardiac risk factors
 - Local Site Toxicity ratings, if incident of phlebitis
 - Local Site Toxicity
 - 0 None
 - 1 Pain
 - 2 Pain & inflammation; phlebitis
 - 3 Ulceration
 - 4 Plastic surgery
- Upon Patient Complaint Or Clinical Event**

Cardiac

- 0 None
- 1 —

At cumulative dose threshold and subsequent intervals

- 2 Asymptomatic, resting ejection fraction decline by >10% baseline, or abnormal cardiac function tests (LVEF >50) with no baseline for comparison
- 3 Mild Congestive Heart Failure, responds to therapy
- 4 Severe/refractory Congestive Heart Failure

For Cardiac Toxicity Ratings:

First rating at the Epirubicin cumulative dose **threshold** of **450m²**, & repeat ratings at each cumulative dose **increment** of **150mg/m²** above threshold (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation)

Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Intermediate Level

CDHA Status Formulary

Pharmacare Status Formulary (red)

Continued Next Page...

EPIRUBICIN**PHARMACEUTICAL CONSIDERATIONS****Injection**

Pharmorubicin RDF: Vials of. Store at room temperature (15-30°C) protected from sunlight. Also contains 0.2 mg methylparaben (to enhance dissolution) and 5 mg lactose per mg epirubicin.

Pharmorubicin PFS: 2 mg/mL clear, red, preservative-free solution. Also contains hydrochloric acid to adjust pH. Store in refrigerator. Protect from sunlight (eg, store in carton until use). The manufacturer recommends discarding the unused portion of vials.

Reconstitute powder with NS or SWI to a final concentration of 2 mg/mL; a slight suspension may form which will completely dissolve on further shaking. Do not use bacteriostatic diluents; early experience with doxorubicin suggested that the use of diluents containing benzyl alcohol results in hypersensitivity reactions. Vials are under negative pressure.

Reconstituted solution for injection

Clear, red solution. Physically stable for 24 hours at room temperature and 48 hours when refrigerated (2-10°C). Protect solutions from direct light. Walker et al reported stability of 150 days of 1 mg/mL and 2 mg/mL solution, when stored at 4 and 23°C in their original vials. Like doxorubicin, epirubicin should not be stored in contact with aluminum but may be safely injected through an aluminum-hubbed needle.

Diluted solution for infusion

Compatible with D5W and NS. Physically stable for at least 7 days refrigerated and stored in the dark. No protection from light is necessary during IV administration of solutions 0.5 mg/mL or greater. After 8 days storage in PVC containers, variable drug loss occurs due to adsorption to the container.

Stability in syringes

A 0.5 mg/mL solution in NS is stable in plastic syringes for at least 28 days if stored below 20°C. A 2 mg/mL solution in sterile water is stable in Plastipak (Becton-Dickinson) plastic syringes for at least 43 days at 4°C.

It is recommended that epirubicin not be mixed with other drugs. Incompatible with heparin.



EPOIETIN

(Colony-Stimulating Factor; Growth Factor)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Eprex® Vials with 4,000IU, 40,000IU, multidose vials with 20,000IU

Keep under refrigeration

MECHANISM OF ACTION

Epoietin induces erythropoiesis by stimulating the division and differentiation of committed erythroid progenitor cells; it induces the release of reticulocytes from the bone marrow into the blood stream, where they mature to erythrocytes in a dose-response manner.

PHARMACOKINETICS

Oral Absorption

inactive orally

Distribution

Onset of action: Several days to 2 weeks

Distributes rapidly in the plasma compartment

highest concentration in liver, kidneys, spleen, lung, bone marrow; excretion in breast-milk unknown

cross blood brain barrier? No

information; may cross placenta

Vd ~4-5% body weight: 21-80mL/Kg (single IV); 57-107mL/Kg (multidose); 42-70mL/Kg (nml HCT)

Metabolism

intact hormone- hepatic metabolism
minimal contribution

desialylated hormone- substantial hepatic clearance via metabolic pathways and/or binding in liver; desialylation and/or removal of oligosaccharide side chains

Excretion

desialylated hormone-biliary excretion is major route (first order)- kidneys, bone marrow spleen

urine- small amounts recovered <10% as unchanged drug

t½ Chronic renal failure: 4-13 hours (higher for first few doses)

IV COMPATIBILITY

no information

ROUTES

direct IV

subcutaneous

EXTRAVASATION HAZARD

no

DOSING

Initial dose: 150 IU/Kg SC tiw; evaluate iron status at baseline and during epoietin treatment

Dose Escalation: if, after 4 weeks of treatment, the hemoglobin increases by <10 g/L or reticulocyte count increases by <40,000 cells/μL, increase dose to 300 IU/Kg for 4 more weeks; if response is not adequate after escalation of dose for 4 weeks, discontinue epoietin

Dose Adjustment: If the hemoglobin increases by >20 g/L/month, decrease epoietin dose by 25%. If hemoglobin exceeds 140 g/L, hold epoietin until hemoglobin returns to 120 g/L, then reinstitute at 25% reduced dose.

- Re-evaluate the need for epoietin when chemotherapy is completed

Adequate trial: 2 months

Pediatric: Safety & effectiveness not established; multiuse vials contain benzyl alcohol and should not be used for neonates or premature infants

Other dosing may be indicated

SIGNIFICANT INTERACTIONS

Continued Next Page...

EPOIETIN

SIDE EFFECTS

* may be life-threatening

side effects in **bold**, *italic* type are common

IMMEDIATE ONSET (hours to days)

- chest pain (7%), tachycardia
- shortness of breath
- nausea (10.5%), vomiting (8%), diarrhea (8.5%)
- anaphylactic reactions (rare)

EARLY ONSET (days to weeks)

- headache (16%), blurred vision
- ***hypertension*** (24%)- increased hematocrit & blood viscosity
- bone pain (11%)

DELAYED/LATE ONSET (weeks-months)

- skin rash, urticaria
- cardiac problems- decreased myocardial oxygenation

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Routine **blood pressure monitoring** during IV infusions, especially in hypertensive patients (or at regular clinic visits while Epoetin therapy is recently started)
- **Hematocrit and iron status (serum ferritin and/or transferrin saturation levels)** monitored regularly

SUGGESTED CRITERIA

- Periodic **neurologic evaluations**, especially during first 90 days of Epoetin therapy

INDICATIONS AND OTHER USES

- Treatment of anemia associated with cancer or chemotherapy in patients with non-myeloid malignancies

PHARMACEUTICAL CONSIDERATIONS

Injection:

Multiple Use vials with 20,000 IU/mL.

Single use vial with 40000 IU/mL.

Single-use prefilled syringes with: 1000 IU/0.5mL, 2000 IU/0.5mL, 3000 IU/0.3mL, 4000 IU/0.4mL, 6000 IU/0.6mL, 8000 IU/0.8mL, 10000 IU/1mL & 40000 IU/1mL

Store in refrigerator at 2-8°C. Do not freeze. Do not shake. Protect from light. Multiple use vials should be discarded within 30 days after first puncture.

GUIDELINES

Visit the **Cancer Care Nova Scotia** website (www.cancercare.ns.ca) for the guideline on Epoetin for treatment of anemia in hematologic malignancies

CONTRAINDICATIONS

- Hypersensitivity to human albumin or mammalian cell-derived products
- uncontrolled hypertension (systolic BP >180 or diastolic BP >90-100mmHg)
- history of porphyria
- unstable angina, recent myocardial infarct, vascular disease
- seizure disorders
- antihypertensive drugs
- iron supplements
- androgens
- desmopressin
- probenecid

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status- Community Level; Take Home Prescription- Indication restrictions CDHA Status Formulary-Restricted* Pharmacare Status

**Restricted to patients under the Nephrology Service; no oncology indications approved*



ESTRAMUSTINE

(Antineoplastic; Hormone (Estrogen/ Nitrogen Mustard)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Emcyt® Off-white capsules with 140mg

Keep in refrigeration

MECHANISM OF ACTION

Exact mechanism of action is unclear. It appears to bind to microtubule proteins, preventing normal tubulin function. Theoretically, the estrogen component serves as a carrier to estrogen-dependent tissues. Whether estramustine actually dissociates to an alkylating moiety in target tissues is speculative; the antitumor effect may be due solely to estrogenic effect. Estramustine causes a marked decrease in plasma testosterone levels, and increase in estrogen levels.

PHARMACOKINETICS

Oral Absorption

75% absorbed, rate and extent of absorption decreased when taken with milk, food or calcium-rich drugs

Distribution

appears to concentrate in prostatic tissue; excretion in breast-milk unknown cross blood brain barrier? no information Vd, PPB- no information

Metabolism

GI-tract: initial dephosphorylation; hepatic: Oxidation and hydrolysis; metabolites include estramustine, estrone, estradiol, nitrogen mustard metabolite(s): active- estradiol, estramustine, estromustine inactive- Yes

Excretion

hepatic: 2.9% to 4.8% as unchanged drug: urine and feces urine: 22-36% in 2-8 days feces: 14-21% in 7 days t½ 20-24 hours

ROUTES

oral

INDICATIONS AND OTHER USES

- Prostate cancer

CONTRAINDICATIONS

- severe liver (hepatic) or heart (cardiac) disease
- blood clots (thromboembolic disorders)
- known hypersensitivity to either estradiol or mechlorethamine

SIGNIFICANT INTERACTIONS

calcium (milk and milk products, calcium supplements, calcium-containing antacids, etc.), food

DOSING

Oral:

- daily: 14 mg/kg/day (ie, one 140 mg capsule for each 10 kg) in 3-4 divided doses
- range: 10-16 mg/kg/day
- Capsules should be taken on an empty stomach (1 hour before or 2 hours after a meal).

Adequate trial: 30 days

Pediatric: Safety & effectiveness not established

Other dosing may be indicated

ESTRAMUSTINE

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)
nausea and vomiting (20-50%)

EARLY ONSET (days to weeks)
impotence or decreased sex drive
(decreased libido)
diarrhea (20-50%)
elevated liver function tests
low WBC (myelosuppression)
skin rash (rare)

DELAYED/LATE ONSET (weeks- years)
breast swelling or tenderness
(gynecomastia, 20-50%)
fluid retention (edema) stroke
congestive heart failure (secondary to edema)
loss of diabetic control (decreased glucose tolerance)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment

SUGGESTED CRITERIA

- Baseline and periodic **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)] and **blood pressure measurement**

PHARMACEUTICAL CONSIDERATIONS

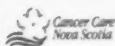
Capsules

Estramustine sodium phosphate 140 mg; store in the refrigerator (2-8°C); keep bottle tightly closed. Bisulfite-, gluten-, lactose- and tartrazine-free.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level Take Home
Prescription (NOTE: Use of
preprinted Physician Standing Order
is recommended)

CDHA Status Formulary
Pharmacare Status Formulary



ETOPOSIDE

(Antineoplastic Agent; Mitotic Inhibitor)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Vepesid® Pink soft-gelatin capsules with 50mg
 Generic products available Vials with 100mg/5mL, 500mg/25mL, 1000mg/50mL-
 to be diluted for infusion

MECHANISM OF ACTION

Etoposide does not inhibit microtubular assembly. It has been shown to delay transit of cells through the S phase and arrest cells in late S or early G2 phase. The drug may inhibit mitochondrial transport at the NADH dehydrogenase level or inhibit uptake of nucleosides into HeLa cells. It is a topoisomerase 2 inhibitor and appears to cause DNA strand breaks.

PHARMACOKINETICS

Oral Absorption

25-74% (mean 48%) bioavailability, large inter- and inpatient variability; absorption not altered by food or other chemotherapy; bioavailability of low oral doses of 100 mg may be better than higher oral doses

Distribution

saliva, liver spleen, kidneys, cardiac tissue and brain tumour tissue cross blood brain barrier? trace CSF-concentration <10% of plasma concentration.

Vd 7-17 L/m², 0.36 L/kg, 28-32% of body weight; Average: 3-36 L/m² PPB 97%, free (unbound) fraction 6-37%

Metabolism

hepatic metabolism to hydroxy acid and cislactone metabolites metabolite(s): active- Yes inactive- Yes

Excretion

elimination described by two - compartment open model, primary route of elimination is renal; 2-16% recovered in feces

urine: 44% of a dose within 72 hours (29% unchanged drug, 15% as metabolites); in children: up to 55% of dose is excreted unchanged in the urine t_{1/2} α IV: 1.5 hrs; po: 0.44 hrs t_{1/2} β IV: 4-11 hours; po: 6.8 hrs Cl 16-39 mL/min/m², 0.68 mL/min/kg; Terminal t_{1/2}- 4-15 hours; Children: 6-8 hours (with normal renal and hepatic function)

ROUTES

oral (usually as single daily dose)
 direct IV (not recommended)
 intermittent IV (over 30-60 minutes)
 continuous IV (BMT)

IV COMPATIBILITY

normal saline, dextrose 5%

EXTRAVASATION HAZARD

IRRITANT

Management- stop IV, aspirate, elevate limb, cold intermittent compresses Follow Extravasation Guidelines

ANTIEMETIC RISK

INTERMEDIATE RISK (10-30% of patients)

- Use a dexamethasone pre-chemotherapy and a dopamine receptor antagonist PRN post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

SIGNIFICANT INTERACTIONS

anticonvulsants, calcium antagonists, carmustine, cyclosporin, cisplatin, cyclosporin, ketoconazole, methotrexate, salicylate, warfarin, other antineoplastic agents

CONTRAINDICATIONS

- known hypersensitivity to etoposide
- pregnancy and breast feeding

Continued Next Page...

ETOPOSIDE

ADMINISTRATION

- Premixed in 500mL bag of Normal Saline; connect piggyback to IV line; Infuse over 30 to 60 minutes; (For doses >200mg, mix in 600mL and infuse over 90 minutes); Adjust rate if blood pressure drops
- Doses usually mixed to a concentration of 0.4mg/mL; may increase concentration up to a maximum concentration of 0.8mg/mL if fluid volume is excessive; if concentration >0.4mg/mL, premixed bag(s) attached to (0.22 micron) in-line filter and administer within 8 hours of preparation. Larger volumes may be used for prehydration of Cisplatin or Ifosfamide dose.
- Take a baseline blood pressure measurement
- Infusion reactions usually controlled by reducing the infusion rate or discontinuation of the drug infusion and administration of vasopressors, corticosteroids, antihistamines and/or plasma volume expanders. Reactions to etoposide may occur with the first treatment dose or subsequent doses and the reaction may begin after only a small portion of the drug has been infused or up to several hours following drug administration. These reactions appear to occur most frequently during the infusion.
- Hypotension may be observed with a rapid infusion rate and as such, it is recommended to administer doses over at least 30-60 minutes. **Vital signs should be monitored during the first 30-60 minutes.**

DOSING

Intravenous:

- q1-4w: 100-250 mg/m²
- q2-5w: 35-150 mg/m²/day x 3-5 days (on consecutive or alternate days)
- 100-150 mg/m²/day x 3-7 days by continuous infusion

Oral:

- Many protocols use IV day 1 and po on subsequent days (eg, days 2-5 or days 3,5). Usual dose is twice the IV dose to the nearest 50 mg.
- daily: 50-100 mg x 1-2 months
- q3-4w: 120-200 mg/m²/day x 5 days given in divided doses
- q4-5w: 50 mg/m²/day x 21 days
- Patients unable to swallow capsules can pierce the capsule and squeeze the contents into pop or juice, mix thoroughly and drink.
- Care givers should use gloves to prepare a solution for the patient.
- A more expensive alternative is to mix the injection with pop or juice.

Bone marrow transplant:

- much higher doses are used for tumour ablation prior to marrow transplant than for standard treatment regimens; eg, 1.2-2.4 g/m² over 17-34 hours or as daily bolus injections may be used in combination with other cytotoxic drugs

Pediatric

Intravenous:

- q3w: 100 mg/m²/day x 5 days
- q3-4w: 100 mg/m²/day x 4 days via continuous infusion
- q3-4w: 150 mg/m²/day x 3 days

Bone marrow transplant:

Doses in children are similar to those for adults, and may be given as 4 hour infusions or continuous infusions. The possibility of precipitation must be considered with longer infusion times.

Other dosing may be indicated

ETOPOSIDE

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)

- * anaphylaxis (33-51%- Symptoms: chills, fever, bronchospasm, dyspnea, tachycardia and hypotension or hypertension)
- vein irritation (phlebitis)
- nausea and vomiting** (30-40%)
- low blood pressure (1-2%, hypotension with rapid IV)
- skin problems (rash, palmar erythema, with high dose)

EARLY ONSET (days to weeks)

- * **low WBC, RBC, platelets (myelosuppression)**, WBC nadir 7-14 days, platelet nadir 9-16 days, recovery 20-28 days)
- hair loss (20-90%, reversible alopecia)
- mouth sores (with high doses, stomatitis)
- loss of appetite (13%, anorexia)
- nerve damage (<1%, peripheral neuropathy)
- liver problems (with high doses, elevated liver function tests)
- metabolic problems (acidosis, with high doses)

DELAYED/LATE ONSET

leukemia

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Clinical assessment of stomatitis:** oral examination upon patient complaint of a sore mouth
- Baseline **blood pressure** at each IV treatment; monitor for hypotension

SUGGESTED CRITERIA

- Baseline & periodic **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- Baseline **renal function tests** (if renal failure suspected) [serum creatinine, electrolytes & BUN]

INDICATIONS AND OTHER USES

- Lung cancer
 - Non-Hodgkin's lymphoma
 - Testicular cancer
- OTHER ONCOLOGY USES**
- Acute lymphocytic leukemia*
Acute myelogenous leukemia
Brain tumours
Cervical carcinoma
Ewing's sarcoma
Gastric carcinoma

- Germ cell tumours*
Gynecologic sarcomas
Hepatocellular carcinoma
Histiocytosis X
Hodgkin's disease
Kaposi's sarcoma
Neuroblastoma
Ovarian cancer
Rhabdomyosarcoma

Continued Next Page...

ETOPOSIDE

PHARMACEUTICAL CONSIDERATIONS

Capsules

50 mg; store at room temperature.

Injection

20 mg/mL (5 mL vial); also contains polyethylene glycol, Tween 80, citric acid, and benzyl alcohol (3%); store at room temperature.

Diluted solution for infusion

- Compatible in D5W or NS. The manufacturer recommends that dilutions be used immediately and that concentrations greater than 0.4 mg/mL not be used as the time to precipitation is highly unpredictable at greater concentrations. Trissel states that a 0.4 mg/mL solution in NS, D5W or Ringer's lactate is physically compatible (less than 5% etoposide loss) for 4 days in glass containers at 21°C. Similar stability in PVC was shown when etoposide was diluted in NS. Concentrations of 0.5 and 0.6 mg/mL in NS in glass containers precipitated at 48 and 24 hours, respectively. Precipitation is unpredictable, depending on concentration, time after dilution, presence of crystallization nuclei, agitation, contact with incompatible surfaces and other factors. Monitor solutions for precipitation before and during administration. The use of non-peristaltic pumps appears to reduce the incidence of precipitation within the tubing during IV administration of etoposide.
- Chemotherapy venting pins constructed of ABS plastic may also crack when used with undiluted etoposide. Cracking of other types of hard plastic devices has been noticed occasionally.
- No loss due to binding was seen when a 0.2 mg/mL solution in NS or D5W was filtered through a 0.22 micron filter.
- Compatible with ondansetron. Some mixtures of etoposide with cisplatin, mannitol and potassium chloride and with cytarabine, daunorubicin, carboplatin, fluorouracil, or ifosfamide have been shown to be compatible for at least 24 hours. It is recommended that etoposide not be mixed with other drugs.

DOSE ADJUSTMENT CRITERIA

Hepatic dysfunction

1. If Bili=26-51 µmol/L or AST=60-180 IU/L, REDUCE to **50%** dose
2. If Bili= 52-85 µmol/L, REDUCE to **25%** dose
3. If Bili >85 µmol/L or AST>180 IU/L, *Omit* dose

Renal dysfunction (Suggested action)

1. If CrCl =12-48 mL/min or Serum Creatinine > 130 µmol/L, REDUCE to **75%** dose
2. If CrCl < 12 mL/min, REDUCE to **50%** dose

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-

Injection- Intermediate Level;

Oral- Basic Level for ordering on preprinted Physician Standing Order

CDHA Status Formulary

Pharmacare Status

Formulary; (red for injectable)

NOTE: It is recommended to limit ordering of this medication to pre-printed Physician Standing Order form, for patient safety

EXEMESTANE

(Antineoplastic Agent, Antimicrotubular, Aromatase Inhibitor) Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Aromasin® Small, light grey tablets

MECHANISM OF ACTION

Exemestane is an irreversible, steroidal aromatase inhibitor. No detectable effect on synthesis of adrenal corticosteroids or aldosterone. It inhibits the activity of aromatase, the principal enzyme responsible for the conversion of androstenedione to estrone, and testosterone to estradiol. Structurally related to androstenedione, one of the usual aromatase substrates, exemestane inactivates the enzyme by irreversibly binding to the active site on aromatase.

PHARMACOKINETICS

Oral Absorption

rapidly and moderately well (about 42%), reaching peak concentrations in ~1 hour, taking after a high fat meal increases the absorption ~ 40%

Distribution

extensive; excretion in breast-milk unknown
cross blood brain barrier? No information
Vd no information

PPB ~90%, primarily to albumin and α -acid glycoprotein

Metabolism

hepatic, oxidation by CYP 450 3A4 followed by reduction, metabolites have little, or no, activity

Excretion

hepatic: 36% to 48% renal: 39% to 45% urine: <1% unchanged
t_{1/2} 24 hours

ROUTES

oral

DOSING

Oral:

- 25 mg PO once daily
 - Administer with food, after breakfast
- Pediatric* Safety & effectiveness not established

Other dosing may be indicated

INDICATIONS AND OTHER USES

- Breast cancer

CONTRAINDICATIONS

- hypersensitivity to exemestane or any component, pregnancy, premenopausal women

SIGNIFICANT INTERACTIONS

estrogen-containing drugs
CYP 3A4 substrate drugs

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)

fatigue (22%), pain (13%), depression (13%), insomnia (11%), anxiety (10%), hot flushes (13%), nausea (18%)

CLINICAL MONITORING

RECOMMENDED CRITERIA

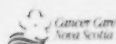
NO RECOMMENDED TOXICITY RATINGS

SUGGESTED CRITERIA

NO ADDITIONAL TOXICITY RATINGS

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status- Community Level
Take Home Prescription (NOTE: Use of preprinted Physician Standing Order is recommended)
CDHA Status Non-Formulary
Pharmacare Status Non-Formulary

**FILGRASTIM**

(Granulocyte Colony Stimulating Factor (G-CSF))

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name Neupogen® Vials with 300..g/1mL & 480..g/1.6mL, injection kit available Keep under refrigeration

MECHANISM OF ACTION

Stimulates the production, maturation, and activation of neutrophils and activates neutrophils to increase both their migration and cytotoxicity

PHARMACOKINETICSOral Absorption

inactive orally

Distribution

rapidly adsorbed following subcutaneous administration. highest concentration in bone marrow. adrenal glands, kidneys, liver ($t_{1/2}$ =0.13-1.1 hrs), excretion in breast-milk unknown

cross blood brain barrier? No information

Vd- 150mL/Kg PPB- No information

Metabolism

systemic

metabolite(s)

active, inactive- No information

Excretion

mainly through liver & kidneys as unchanged filgrastim- individual variation?

Urine No information

$t_{1/2}$ 1.8-7 hours Cl- 0.5-0.7mL/min

IV COMPATIBILITY

5% dextrose 5% dextrose + human albumin

ROUTES

subcutaneous (rotate sites)
direct intravenous (over 30 minutes)
continuous intravenous over 24 hours or 11-20 days

DOSINGIV/SC

- daily 5 mcg/kg or 200 mcg/m² for up to 2 weeks or until the ANC reaches $1 \times 10^9/L$ following the expected nadir
 - Treatment should be continued if the patient has clinical signs of infection does not have a rising ANC or is in a situation in which persistent marrow compromise is suspected
 - May be increased by 5 mcg/kg each chemotherapy cycle depending on response
 - Discontinuation usually results in a 50% drop in circulating neutrophils within 1-2 days, with a return to pretreatment levels in 1-7 days. Therapy should be discontinued if the absolute neutrophil count (ANC) surpasses $10 \times 10^9/L$ after the ANC nadir has occurred to avoid potential risks of excessive leukocytosis
 - Dose can be rounded off to 300 or 480 mcg to avoid wastage
- Pediatric:* Dosing the same as for adults

Other dosing may be indicated

INDICATIONS AND OTHER USES

- Rescue of febrile neutropenic patients
- Prevent neutropenia which interferes with potentially curative chemotherapy
- Stimulate engraftment post BMT

OTHER ONCOLOGY USES

Aplastic anemia

Augment peripheral blood stem cell harvest

Chronic benign cyclical neutropenia

Myelodysplastic syndrome

CONTRAINDICATIONS

- Do not administer within 24 hours before or after last dose of chemotherapy, or within 12 hours before or after radiotherapy
- known hypersensitivity to E. coli derived products

SIGNIFICANT INTERACTIONS

concurrent chemotherapy or radiotherapy, cyclophosphamide, lithium, non-narcotic analgesics, topotecan, vincristine, other antineoplastic agents

Continued Next Page

FILGRASTIM

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET

(hours to days)

EARLY ONSET

(days to weeks)

arthralgia, myalgia

headache

dull pain in long bones, back, pelvis

(first 2-3 days of treatment)

pain at injection site, vasculitis

allergic or anaphylactic reaction

skin rash (Sweet's syndrome & other

dermatoses)

increased serum uric acid, LDH, alkaline

phosphatase, LAP

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Monitor consecutive complete blood count including differential (CBC) results at least 1-2 times weekly

SUGGESTED CRITERIA

- Periodic clinical assessment of cardiac function (if pre-existing cardiac condition)
- Baseline & periodic hepatic function tests (if impairment suspected) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- Baseline & periodic renal function tests (if impairment suspected) [serum creatinine, electrolytes & BUN]

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status- Basic Level for ordering Take Home Prescription

Indication restriction- Provincial Cancer Drug Formulary

CDHA Status Formulary-Indication restrictions

- secondary prophylaxis of febrile neutropenia in patients with prior episode FN subsequent to chemotherapy;
- patients unable to tolerate chemotherapy due to dose reduction or delay, where dose intensity is important;
- chronic neutropenia;
- patients prior to peripheral blood cell collection;
- following autologous transplant, patients receiving allogeneic BMT to accelerate engraftment;
- patients with drug induced neutropenia from AIDS therapy;
- patients with chronic neutropenia while awaiting BMT (e.g. myelodysplastic disorders, aplastic anemia);
- primary prevention with standard chemotherapy where there is $\geq 50\%$ febrile neutropenia rate (documented)

Pharmacare Status Non-Formulary- Special funding program operated by QEII HSC Pharmacy

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FILGRASTIM

PHARMACEUTICAL CONSIDERATIONS

Injection

300 mcg/mL clear, colourless liquid in 1 mL (300 mcg) and 1.6 mL (480 mcg) vials, preservative-free; contains sodium acetate as a buffer, 0.004% Tween 80 and mannitol 50 mg per mL. Store in refrigerator (2-8°C). May be allowed to reach room temperature for up to 24 hours. Freezing or storage at temperatures greater than 30°C results in aggregate formation and solutions stored under such conditions should not be used. Avoid vigorous shaking. Discard unused portions of vials and vials left at room temperature for more than 24 hours.

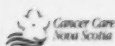
Diluted solution for infusion

Incompatible with NS. When administering filgrastim through IV lines that have been used to infuse saline, the lines should be flushed with D5W before and after filgrastim administration. Compatible with D5W in PVC, polyolefin and propylene containers. For dilutions below 15 mcg/mL, albumin to a final concentration of 2 mg/mL or more must first be added to the D5W to prevent adsorption of filgrastim to the infusion container walls. Filgrastim should not be diluted to less than 2 mcg/mL even in the presence of albumin. Dilutions in D5W, with or without albumin, are physically stable for up to 7 days refrigerated (2-8°C) or at room temperature below 30°C. However, because the solution contains no preservative, the manufacturer recommends using dilutions within 24 hours.

Stability in syringes

Undiluted filgrastim in Becton-Dickinson tuberculin syringes is physically stable for 7 days refrigerated (2-8°C) or 24 hours at room temperature below 30°C. However, because the solution contains no preservative, the manufacturer recommends that prefilled syringes be refrigerated and used within 24 hours.

It is recommended that filgrastim not be mixed with other drugs. Incompatible with saline solution.



FLUDARABINE

(Antineoplastic Agent, Antimetabolite)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Fludara® Vials with 50mg/2mL. Tablets with 10 mg Fludarabine Phosphate

MECHANISM OF ACTION

Fludarabine appears to inhibit DNA synthesis by interference with DNA polymerase, ribonucleotide reductase, and adenosylmethionine

PHARMACOKINETICS

Oral Absorption

50-65% bioavailable (oral tablets)

Distribution

widely distributed. Vd suggests significant degree of tissue binding; excretion in breast-milk unknown; cross blood brain barrier? Yes

Vd 36-96 L/m²; children: 10.8 L/m²

PPB no information

Metabolism

Hepatic uptake, rapidly dephosphorylated in plasma to 2-fluorovidarabine (2-FLAA) and 2-fluoroadenine-5-triphosphate which is necessary for cellular uptake; metabolite(s): active- 2-F-ara-ATP; inactive- Yes

Excretion

excreted by kidneys

urine: 60% within 24 hours, 24% as the metabolite

t_{1/2t} 0.6-1.64 hours (some studies showed rapid initial distribution phase of 5-7 minutes); children: 1.6 hours

t_{1/2β} 8-12.4 hours; children: 18.7 hours

Elimination t_{1/2} 10-30 hours

Cl- 8.9 L/hr, 9.1 L/h/m²;

children: 0.7 L/h/m²

IV COMPATIBILITY

normal saline, dextrose 5%

ROUTES

direct IV (intermittent infusion preferred)

intermittent IV (preferred, in 50-125 mL over 30-60 minutes)

ADMINISTRATION

continuous IV

(increased myelosuppression)

- Mix in 50mL minibag (Normal Saline); Infuse over 15-30 minutes

DOSING

Intravenous:

- q4-5w: 25 (18-30) mg/m²/day x 5 days
- q4w: 20 mg/m² bolus followed by
- 30 mg/m²/day x 2 days by continuous infusion

Oral:

- q4w: 40 mg/m² PO daily for 5 days

Pediatric

Intravenous: (phase I/II trial)

- 8 mg/m² loading dose followed by 23.5 mg/m²/day x 5 days by continuous infusion

Other dosing may be indicated

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

nausea and vomiting (36%, mild to moderate)

fever (60%), chills, fatigue

rash

increased uric acid levels

(hyperuricemia)

EARLY ONSET (days to weeks)

- * **low WBC, RBC, platelets** (**myelosuppression**, nadir 13-16 days, recovery 37-45 days)
- diarrhea
- mouth sores (stomatitis)
- increased liver function tests

DELAYED/LATE ONSET (weeks to years)

- * nerve problems (peripheral neuropathy, rare)
- lung problems (interstitial pneumonitis, rare)

Continued Next Page...

FLUDARABINE

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum uric acid levels before each cycle of treatment
- Watch for symptoms of fever or infection
- Periodic clinical pulmonary exam, including auscultation, pulmonary toxicity ratings (SOB)

SHORT OF BREATH

- 0 No change
- 1 Mild Shortness of Breath
- 2 Dyspnea on exertion
- 3 Dyspnea at normal level of activity
- 4 Dyspnea at rest

Rated At Periodic Clinic Visits And
in Response To Patient Complaints

SUGGESTED CRITERIA

- Periodic renal function tests [serum creatinine, electrolytes & BUN]
- Baseline liver function tests [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels, serum albumin]
- Infection rating if clinical evidence of opportunistic infection

INFECTION

- 0 None
- 1 Mild; no active treatment
- 2 Moderate; localized; active treatment required
- 3 Severe; systemic infection; parenteral antibiotics
- 4 Life threatening sepsis

Rated Upon Clinical Indication Of
Infection

EXTRAVASATION HAZARD

None

ANTIEMETIC RISK

LOW RISK (Less than 10% of patients)

- No routine antiemetic pre-chemotherapy or post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

SIGNIFICANT INTERACTIONS

- cytarabine, pentostatin, other antineoplastic agents, warfarin

DOSE ADJUSTMENT CRITERIA

Renal dysfunction

1. If CrCl = 30-72mL/min, REDUCE to 50% dose
2. If CrCl < 30mL/min, OMIT dose

GUIDELINES

Visit the **Cancer Care Nova Scotia** website (www.cancercare.ns.ca) for the guideline on Fludarabine for acute leukemia

INDICATIONS AND OTHER USES

- Chronic lymphocytic leukemia

OTHER ONCOLOGY USES

Hairy cell leukemia

Non-Hodgkin's lymphoma

Mycosis fungoides

CONTRAINDICATIONS

- pregnancy and breast feeding

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Injection- Basic Level

Oral- Community Level: Take Home prescription (NOTE: Use of preprinted Physician Standing Order is recommended)

Indication restriction- Provincial
Cancer Drug Formulary

CDHA Status

Formulary- Restricted to Hematology
Guidelines

Pharmacare Status Non-Formulary

NOTE: It is recommended to limit ordering of this medication to preprinted Physician Standing Order form, for patient safety

Continued Next Page...

FLUDARABINE**PHARMACEUTICAL CONSIDERATIONS****Injection**

50 mg vial; contains mannitol and sodium hydroxide to adjust pH. Store in refrigerator.

Reconstitute powder with 2 mL SWI to a final concentration of 25 mg/mL.

Reconstituted solution for injection

Physically and chemically stable for at least 24 hours at room temperature and 48 hours if refrigerated. Less than 2% decomposition in 16 days at 25°C under normal room lighting conditions has been reported. The manufacturer recommends that unused solutions be discarded 8 hours after reconstitution since they contain no preservatives.

Diluted solution for infusion

May be further diluted with D5W or NS to a final concentration of 1 mg/mL. Such dilutions are reported to undergo less than 3% decomposition in 16 days at room temperature and normal room lighting conditions. Little or no loss occurred when a 0.04 mg/mL solution in D5W or NS was stored for 48 hours at room temperature or refrigerated.

It is recommended that fludarabine not be mixed with other drugs.

Oral Tablets

Film-coated tablets with 10 mg fludarabine phosphate. Store at room temperature (15-30°C). Do not freeze. Leave contents in protective packaging until use.

May be taken on an empty stomach or with food. Swallow tablets whole- do not crush or chew.

FLUOROURACIL

(Antineoplastic Agent; Antimetabolite)

Revision Date: Feb 03

DRUG

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Adrucil®

Vials with 500mg/10mL, 5000mg/100mL

Generic products available

Do **NOT** Refrigerate

MECHANISM OF ACTION

5-Fluorouracil is a fluorinated pyrimidine antimetabolite. The nucleotides generated intracellularly exert a cytotoxic effect by inhibiting thymidylate synthase (TS) resulting in inhibition of DNA synthesis. Incorporation into RNA also interferes with RNA synthesis and function.

PHARMACOKINETICS

Oral Absorption

Varies from 28-100% as a result of dihydropyrimidine dehydrogenase (DPD). Oral 5-FU is not generally used, but is being investigated in combination with inhibitors of DPD.

Distribution

into all body water by passive diffusion, crosses placenta, high and persistent levels in malignant effusions; excretion in breast-milk unknown cross blood brain barrier? Yes

Vd- 0.25 L/kg, 8.84 L/m²;

12-89% of body water, 13-18 L

PPB 8-12%

Metabolism

intracellular (anabolic) to active nucleotides (FdUMP, FUTP)
hepatic and extrahepatic (catabolic) via DPD to dehydrofluorouracil (DHFU) which is subsequently metabolized to fluoro-β-alanine (FBAL)

metabolite(s): inactive- Yes

active- Yes (FdUMP, FUTP)

Excretion

excreted as respiratory CO₂, 5%
excreted unchanged in urine; the majority of the drug is eliminated by metabolism

urine: <5% unchanged

t_{1/2}- 8-13 minutes

Cl- 0.6-2.3 L/min, 16 mL/min/kg,

women 155 L/h/m², men 179 L/h/m²

EXTRAVASATION HAZARD

vein pigmentation (rare);

thrombophlebitis (rare)

IV COMPATIBILITY

normal saline, dextrose 5%

ROUTES

direct IV (over 1-2 minutes)
intermittent IV (in 50-100 mL over 10-30 minutes)
continuous IV (improved therapeutic index over direct IV)

ADMINISTRATION

- Slow push through sidearm of free flowing IV (5% Dextrose, Normal Saline) over 1-2 minutes (*administering nurse should be certified to administer IV push chemotherapy agents*)

- May be given by direct IV push, followed by a Normal Saline flush, if no IV line has been set up

- May be mixed in 50mL minibag (5% Dextrose, Normal Saline); Infuse through sidearm of free flowing IV over 10-15 minutes

For inpatient administration:

- Mix dose in 1000mL Normal Saline, infuse at over specified time

Fluorouracil Infusion

- **Continuous infusion** using ambulatory infusion pump
- Infuse through central venous access device or PICC line, if available
- Infuse through patent peripheral venous catheter, if infusion for only 3-5 days; Inspect peripheral infusion sites daily and replace if evidence of irritation or extravasation
- Protect from light

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FLUOROURACIL

SIDE EFFECTS

* may be life-threatening

side effects in **bold**, *italic* type are common

IMMEDIATE ONSET (hours to days)

- * anaphylaxis (rare- Symptoms: angioedema, hypotension)
vein irritation (phlebitis)
- nausea and vomiting*** (usually mild)
- eye problems (lacrimation, conjunctivitis)
- * heart problems (rare, angina pectoris, ECG changes)
- radiation recall reaction (rare)
- reddening of skin*** (topical use, erythema)

EARLY ONSET (days to weeks)

- * ***low WBC, RBC, platelets (myelosuppression)***, nadir 7-14 days, recovery 22-24 days)
- mouth sores*** (stomatitis, may be severe with high dose leucovorin)
- * ***diarrhea*** (may be severe with high dose leucovorin)
- hair loss (alopecia, usually mild)
- skin problems (hyperpigmentation, photosensitivity, rash, nail changes, hand-foot syndrome)
- eye problems (lacrimation)
- blood problems (megaloblastosis)
- central nervous system problems (acute cerebellar syndrome, acute encephalopathy)
- reddening, blistering of skin*** (topical use)

DELAYED/LATE ONSET (weeks to years)

- radiation recall reaction (rare)
- eye problems (tear duct fibrosis)
- central nervous system problems (acute cerebellar syndrome, acute encephalopathy)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth

For Continuous Infusion:

- **Skin assessment**, especially extremities

**Upon Patient Complaint
Or Clinical Event**

SUGGESTED CRITERIA

- Baseline **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels, serum albumin] (if severe organ failure suspected)
- Baseline **renal function tests** [serum creatinine, electrolytes & BUN] (if severe organ failure suspected)

For Continuous Infusion:

Local Site Toxicity ratings, if incident of phlebitis

LOCAL SITE TOXICITY

- 0 None
- 1 Pain
- 2 Pain & inflammation, phlebitis
- 3 Ulceration
- 4 Plastic surgery

Continued Next Page...

FLUOROURACIL

DOSING

IV bolus:

- 450 mg/m²/day x 5 days then on day 29: 450 mg/m² q1w
- q1w: 350-600 mg/m²
- q3w: 600 mg/m²
- q3-4w: 250-600 mg/m²/day x 5 days
- q4w: 400-500 mg/m² days 1 & 8

IV infusion:

- q1w: 2.6 g/m² over 24 hours
- q1w: 30 mg/kg/day x 2 days
- q3-4w: 400-1000 mg/m²/day x 4-10 days as continuous infusion
- daily: 200-300 mg/m² x 5-18 weeks as continuous infusion

Pediatric

IV bolus: q3w: 600 mg/m²

IV infusion: q3w: 800-1200 mg/m²
continuous IV over 24-120 hours

Other dosing may be indicated

INDICATIONS AND OTHER USES

- Actinic keratosis
- Bladder cancer
- Breast cancer
- Cervical cancer
- Colorectal cancer
- Gastric cancer
- Head and neck cancer
- Ovarian cancer
- Pancreatic cancer
- Prostate cancer

OTHER ONCOLOGY USES

Hepatic cancer

Endometrial cancer

Lung cancer, non-small cell

CONTRAINDICATIONS

- pregnancy and breast feeding
- low WBC, RBC, platelets (myelosuppression)

ANTIEMETIC RISK

LOW RISK (Less than 10% of patients)

- No routine antiemetic pre-chemotherapy or post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

DOSE ADJUSTMENT CRITERIA

Marked hepatic dysfunction:

Omit dose if bilirubin elevated above 85µmol/L

(Suggested action)

SIGNIFICANT INTERACTIONS

allopurinol, amifostine, calcium folinate, cimetidine, leucovorin, metronidazole, morphine, pyridoxine, sorivudine, thiazide diuretics, warfarin, other antineoplastic agents

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Basic Level

CDHA Status Formulary

Pharmacare Status Formulary (red)

FLUOROURACIL

PHARMACEUTICAL CONSIDERATIONS

Topical preparations

1% topical solution; 1% or 5% cream. store at room temperature.

Injection

50 mg/mL (5 mL, 10 mL, 50 mL and 100 mL vial or amp). Clear, colourless to faint yellow solution; preservative-free. May contain sodium hydroxide for pH adjustment. Store at room temperature protected from intense incandescent light and sunlight. If a precipitate occurs due to storage at low temperature, resolubilize by heating to 60°C with vigorous shaking and allow to cool to body temperature before using. Although slight discolouration does not affect potency, a dark yellow indicates greater decomposition and such solutions should not be used.

Solution for injection

One manufacturer (Pharmacia) recommends that unused portions of vials be discarded within 8 hours of puncture, since the solution is preservative-free.

Stability in syringes

Fluorouracil does not adsorb to polypropylene syringes or polyethylene syringe plungers. Benvenuto reported that fluorouracil in D5W was stable for at least 30 days at room temperature in plastic syringes. One manufacturer (Pharmacia) recommends that syringes be stored at room temperature and used within 24 hours of withdrawal from vials.

Undiluted solution in ambulatory pumps

Under simulated ambulatory infusion conditions, three brands of undiluted fluorouracil, including the Roche brand, demonstrated stability of 7 days at 37°C in portable infusion pump reservoirs (Pharmacia Deltec CADD-1, Model 5100, Cormed II, Model 10500, Medfusion Infused 200, and Pancretect Provider I.V., Model 2000). However, the Roche brand at 25°C demonstrated a fine precipitate 48-96 hours after pumping action began.

Diluted solution for infusion

Solutions of 1-2 g/L NS, D5W and dextrose-saline in glass and PVC containers were physically and chemically stable for 8 weeks at room temperature in the dark and exposed to fluorescent light. A higher concentration (8 g/L) in D5W was stable for only 7 hours in glass containers but for 43 hours in PVC containers. Fluorouracil apparently does not adsorb to PVC, polyethylene or silastic containers or tubing but may be extensively adsorbed to glass containers.

Fluorouracil (Roche) 500 mg/50 mL in D5W in a PVC reservoir of an ambulatory infusion pump (Travenol PL 145 MVP) demonstrated little change in drug content in 7 days at 25°C, but drug concentration increased progressively over 16 weeks (probably due to water evaporation from the bag). No change was seen when the reservoirs were stored for 16 weeks at 5°C. Fluorouracil (Roche) 500 mg/60 mL in D5W in an elastomeric reservoir (Travenol Infusor) exhibited less than 10% loss after 16 weeks' storage at 5°C.

Filtration

Little or no loss of fluorouracil 10-75 mcg/mL was seen when the solution was filtered through either cellulose nitrate/cellulose acetate ester (Millex OR) or Teflon (Millex FG) filters.

Some admixtures with heparin, leucovorin or prednisolone sodium phosphate may be compatible. It is recommended that fluorouracil not be mixed with other drugs.

Incompatible with carboplatin, cisplatin, cytarabine, diazepam, doxorubicin, epirubicin, methotrexate and ondansetron.

FLUTAMIDE

(Antiandrogen; Antineoplastic Agent)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Euflex® Yellow tablets with 250mg Flutamide;

Generic products available

MECHANISM OF ACTION

Flutamide acts as an antiandrogen by inhibiting androgen uptake and/or inhibiting nuclear binding of androgen to target tissues.

PHARMACOKINETICS

Oral Absorption

rapid and complete

Distribution

not defined

cross blood brain barrier? no information

Vd- no information PPB- parent

drug: 94-96%; Metabolite: 92-94%

Metabolism

hepatic; primary metabolite: 2-

hydroxyflutamide (active); 10 other

metabolites identified

metabolite(s): inactive- yes

active- 2-hydroxyflutamide

Excretion

primarily in kidneys; feces

Urine: 28% in 24 hours; 96% within 3 days

$t_{1/2} \alpha$ - 5-6 hours

$t_{1/2} \beta$ - 9.6 hours; 2-hydroxyflutamide: 5-6 hours

ROUTES

oral

INDICATIONS AND OTHER USES

- Prostate cancer

CONTRAINDICATIONS

- known hypersensitivity to flutamide

SIGNIFICANT INTERACTIONS

warfarin

Cytochrome P450 Substrate

DOSING

Oral: daily; 250 mg po tid

Pediatric: No pediatric indications

PHARMACEUTICAL CONSIDERATIONS

Tablets: 250 mg; store at room temperature. Tablets contain cellulose, lactose, magnesium stearate, starch, silica gel and sodium lauryl sulfate.

Tartrazine-free.

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)

nausea and vomiting (rare)

EARLY ONSET (days to weeks)

breast swelling or soreness

(***gynecomastia*** 61%)

leaking from the nipple (galactorrhea)

appetite or bowel changes

fatigue

DELAYED/LATE ONSET (weeks- years)

fluid retention (edema)

blood clots (thromboembolism)

heart attack (myocardial infarction, rare)

depression

liver problems (elevated hepatic function tests)

blurred vision (rare)

reduced sperm counts

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-

Community Level: Take Home

Prescription (NOTE: Use of pre-printed Physician Standing Order is recommended)

CDHA Status Formulary

Pharmacare Status Formulary

CLINICAL MONITORING

SUGGESTED CRITERIA

- Periodic **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)], then repeat monthly for first 4 months, then periodically thereafter or as indicated for symptomatic liver dysfunction



GEFITINIB

(Signal Transduction Inhibitor- Tyrosine Kinase)

Revision Date: Oct 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: IressaTM Brown tablets with 250 mg of Gefitinib

Other Name: ZD 1839

MECHANISM OF ACTION

Gefitinib is a protein-tyrosine kinase inhibitor which inhibits tyrosine kinase associated with epidermal growth factor receptor EGFR. EGFR is expressed on the cell surface of both normal and cancer cells. To date, no clinical study has demonstrated a correlation between EGFR expression and response to gefitinib. Gefitinib has been tested in numerous cancers, particularly non-small cell lung cancer.

PHARMACOKINETICS

Oral Absorption

Slowly absorbed- 60% mean oral bioavailability, not affected by food

Distribution

Gefitinib distributed extensively through the body, with peak plasma levels 3-7 hours after oral dose.

Vd- 1400L (IV dose)

PPB- approximately 90%, mostly to albumin and α_2 -acid glycoprotein.

Metabolism

Extensive hepatic metabolism by cytochrome P450 enzymes, mostly CYP3A4.

Biotransformation pathways: metabolism of N-propoxymorpholino-group, demethylation of methoxyl group on quinazoline, oxidative defluorination of ha:ogenated phenyl group
metabolite(s): active- O-demethyl gefitinib inactive- four others

Excretion

Cleared in the liver, excreted predominately in the feces

Feces: 88% of dose Urine: 4% of dose
t $\frac{1}{2}$ - 48 hours. CI 595 mL/min

total plasma

INDICATIONS AND OTHER USES

US Indication: Locally advanced or metastatic non-small cell lung cancer, after failure with platinum-based and docetaxel chemotherapy

CONTRAINDICATIONS

- patients with hypersensitivity to Gefitinib or to any other component of Iressa.

ROUTES

Oral

ADMINISTRATION

- Gefitinib is taken orally, with or without food.

SIGNIFICANT INTERACTIONS

- Drugs that may **increase** Gefitinib plasma concentrations: **CYP3A4 Inhibitors** (e.g., ketoconazole, itraconazole, erythromycin, clarithromycin): Gefitinib co-administered with a single dose of itraconazole- significant increase in exposure to imatinib (mean AUC increased by 88%)
- Drugs that may have their plasma concentration **altered** by Gefitinib: **CYP3A4 Substrates** (e.g., simvastatin, warfarin, cyclosporine or pimozide); INR elevation and bleeding disorders with patients taking warfarin and gefitinib concurrently.
- Drugs that may **decrease** Gefitinib plasma concentrations: **CYP3A4 Inducers** (e.g., dexamethasone, phenytoin, carbamazepine, rifampicin, phenobarbital or St. John's Wort): Induction of CYP3A4 by rifampicin decreased Gefitinib AUC by 85%.
- Drugs that may decrease Gefitinib oral absorption by reduction of gastric acid (e.g. high doses of ranitidine, sodium bicarbonate) reduce Gefitinib AUC

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GEFITINIB

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

EARLY ONSET

(days to weeks)

EARLY ONSET

(continued)

diarrhea (48%)

skin rash (43%)

nausea (13%) and **vomiting** (12%)

acne (25%), **dry skin** (13%)

pruritis (8%), **anorexia** (7%), **asthenia**

(6%), **weight loss** (3%)

* **interstitial lung disease** (1%)- acute

onset dyspnea with cough or low grade
fever, rapid progression

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- Baseline & periodic **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- Check for **edema** at each visit

SUGGESTED CRITERIA

- Toxicity ratings of Lethargy and Edema at treatment review visit
- LETHARGY**
0. None
 1. Mild (Performance Status decreased by 1)
 2. Moderate (Performance Status decreased by 2)
 3. Severe (Performance Status decreased by 3)

DOSING

Oral: daily: 250 mg po daily (higher doses do not give better response but increase toxicity)

Pediatric: No pediatric indications

Other dosing may be indicated

EMERGING INFORMATION

This drug is under investigation and has not been widely used in oncology practice. As new information is discovered, portions of this monograph may become outdated. Refer to primary literature and revisions to official product monograph to ensure that information on this drug is current.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-

Community Level: Take Home

Prescription (NOTE: Use of pre-

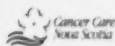
printed Physician Standing Order is recommended)

CDHA Status

Non-Formulary

Pharmacare Status

Non-Formulary

**GEMCITABINE**

(Antineoplastic Agent, Antibiotic)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Gemzar® Vials with 200mg & 1000mg Gemcitabine for reconstitution

MECHANISM OF ACTION

Gemcitabine is a pyrimidine antimetabolite that inhibits DNA synthesis through inhibition of DNA polymerase and possibly ribonucleotide reductase. It is specific for the S phase of the cell cycle.

PHARMACOKINETICSOral Absorption

no information

Distribution

affected by duration of infusion and patient gender

cross blood brain barrier? no information

Vd- short infusion- 50L/m², long infusion- 370L/m² PPB- very low (<10%)

Metabolism

intracellular, hepatic via nucleoside kinases & deamination
metabolite(s) active- gem-diphosphate & gem-triphosphate
inactive- uracil metabolite

Excretion

renal: 99% 92-98% as the inactive uracil metabolite or unchanged

gemcitabine, fecal: <1%

urine: yes

t_{1/2} short infusions- 32-94min, long infusions- 4-10 hours (depends on age & gender)

Cl depends on age & gender: 69.4 to 30 7L/hr/m²; 92.2 to 40 7L/hr/m² (29-79 years)

ANTIEMETIC RISK

INTERMEDIATE RISK (10-30% of patients)

- Use a dexamethasone pre-chemotherapy and a dopamine receptor antagonist PRN post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

SIGNIFICANT INTERACTIONS

amphotericin, immunosuppressants (e.g. azathioprine, steroids, cyclophosphamide, cyclosporin, tacrolimus) radiation therapy, warfarin, other antineoplastic agents

IV COMPATIBILITY

0.9% sodium chloride

ROUTES

intravenous infusion over 30 minutes

ADMINISTRATION

- Mix drug in 100mL bag (Normal Saline); Infuse over 30 minutes through free-flowing IV
- Protect from light

EXTRAVASATION HAZARD

injection site reactions (4%); no reports of injection site necrosis

DOSING

Intravenous

2 weeks

- 2500 mg/m² (range 1250-2500 mg/m²) IV for one dose on day 1

3 weeks

- 1250 mg/m² (range 800-1250 mg/m²) IV for one dose on days 1 and 8
- (total dose per cycle 2500 mg/m² [range 1600-2500 mg/m²])

4 weeks

- 1000 mg/m² (range 500-1250 mg/m²) IV for one dose on days 1, 8 and 15
- (total dose per cycle 3000 mg/m² [range 1500-3750 mg/m²])

8 weeks

- 1000 mg/m² (range 500-1000 mg/m²) IV for one dose on days 1, 8, 15, 22, 29, 36 and 42 for the first cycle; then continue with the 4-week dose schedule (see above)
- (total dose per 8-week cycle 7000 mg/m² [range 3500-7000 mg/m²])

Pediatric No pediatric indications

Other dosing may be indicated

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GEMCITABINE

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET

(hours to days)

nausea, vomiting

diarrhea

headache

EARLY ONSET

(days to weeks)

* **myelosuppression**

flu-like symptoms, lethargy,

myalgia

anorexia

edema

pulmonary symptoms (e.g. cough,

hemoptysis, chest pain, dyspnea)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Check for **edema** at each visit
- Routine toxicity ratings of Flu-like Symptoms. Lethargy at each visit

LETHARGY

- 0 None
- 1 Mild (Performance Status decreased by 1)
- 2 Moderate (Performance Status decreased by 2)
- 3 Severe (Performance Status decreased by 3)

FLU-LIKE SYMPTOMS

- 0 None (**Arthralgia, myalgia,**
- 1 Mild **diaphoresis, rigours/**
- 2 Moderate **chills**)
- 3 Severe **Rated At Each Clinic Visit**

SUGGESTED CRITERIA

- Baseline & periodic **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- Baseline & periodic **renal function tests** (if renal failure suspected) [serum creatinine, electrolytes & BUN]

EDEMA

- 0 None
- 1 1+ or dependant evening only
- 2 2+ or dependant throughout the day
- 3 3+
- 4 4+ generalized anasarca

Rated If Edema Noted On Routine Visits

INDICATIONS AND OTHER USES

- Lung cancer, non-small cell
- Pancreatic cancer

OTHER ONCOLOGY USES

Breast cancer

Cervical Cancer

Bladder cancer

Head and neck cancer

Lung cancer, small cell

Lymphoma, cutaneous T-cell

Lymphoma, Hodgkin's disease

Mesothelioma

Ovarian cancer

CONTRAINDICATIONS

- bone marrow depression, infection
- bone marrow depressants, radiation therapy

GEMCITABINE

PHARMACEUTICAL CONSIDERATIONS

Injection. 200 mg and 1000 mg vials (as the hydrochloride salt). Store at room temperature.

Reconstitute 200 mg vial with 5 mL of NS without preservative and 1000 mg vial with 25 mL of NS without preservative to yield a gemcitabine concentration of 38 mg/mL. Reconstitution of concentrations greater than 40 mg/mL may result in incomplete dissolution and should be avoided. 39 Reconstituted solution is stable for 24 hours at room temperature and should not be refrigerated due to the possibility of crystal formation.

Diluted solution for infusion. May be further diluted with NS to concentrations as low as 0.1 mg/mL. 4 Diluted gemcitabine solution is physically and chemically stable for up to 35 days at room temperature and under refrigeration. 40 However, the manufacturer recommends that the admixture be used within 24 hours since the solution does not contain preservatives. 31

Bacterial challenge. Gemcitabine 2.4 mg/mL diluted in NS did not exhibit a substantial antimicrobial effect on the growth of four organisms inoculated into the solution. Diluted solutions should be stored under refrigeration whenever possible and that the potential for microbiological growth should be considered when assigning expiration periods.

Compatibility. The following are compatible via Y-site injection: amifostine, bleomycin, carboplatin, carmustine, cisplatin, cyclophosphamide, cytarabine, dactinomycin, daunorubicin, dexamethasone, dexrazoxane, diphenhydramine, docetaxel, dopamine, doxorubicin, etoposide, fludarabine, fluorouracil, granisetron, heparin, hydrocortisone, hydromorphone, idarubicin, ifosfamide, leucovorin, lorazepam, mannitol, meperidine, mesna, metoclopramide, mitoxantrone, morphine, ondansetron, paclitaxel, plicamycin, potassium chloride, ranitidine, sodium bicarbonate, streptozocin, teniposide, thiotepe, topotecan, vinblastine, vincristine, vinorelbine.

Incompatibility. The following are incompatible via Y-site injection: furosemide, irinotecan, methotrexate, methylprednisolone, mitomycin, prochlorperazine.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Basic Level; Indication restriction-
Provincial Cancer Drug Formulary
CDHA Formulary Status-Formulary-
Restricted
Pharmacare Formulary Status-
Non-Formulary

GOSERELIN

(Hormone (Gonadotropin Hormone-Releasing Antigen))

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Zoladex® SC Applicator with 3.6mg Goserelin implantation rods
Zoladex LA® SC Applicator with 10.8mg Goserelin implantation rods

MECHANISM OF ACTION

Synthetic analog of luteinizing-hormone-releasing hormone (LHRH). Following an initial increase in luteinizing hormone (LH) and follicle stimulating hormone (FSH), chronic administration of goserelin results in a sustained suppression of pituitary gonadotropins. Serum testosterone falls to levels comparable to surgical castration. The exact mechanism of this effect is unknown, but may be related to changes in the control of LH or down-regulation of LH receptors.

PHARMACOKINETICS

Oral Absorption

inactive orally

Distribution

goserelin is rapidly absorbed following subcutaneous administration
cross blood brain barrier? no information
Vd- male: 44.1 L, female: 20.3 L
PPB- poorly protein bound <30%

Metabolism

hepatic

metabolite(s) active, inactive- no information

Excretion

renal (90%) as unchanged goserelin (20%)
urine: yes as unchanged goserelin (20%)
t_{1/2} - 4-5 hours, prolonged to 12 hours with severely impaired renal function
Cl- 1.9-8 L/hour

ROUTES

SC implant into the stomach
SC (anterior abdominal wall preferred), may use local anesthetic, such as lidocaine 1% without epinephrine or EMLA cream if injection uncomfortable

DOSING

SC:

- q28d: 3.6 mg, depot releases approximately 120 mcg/day
- q84d: 10.8 mg
- A delay of a few days is permissible.

Pediatric: No pediatric indications

Other dosing may be indicated

INDICATIONS AND OTHER USES

- Prostate cancer

OTHER ONCOLOGY USES

Breast cancer

SIGNIFICANT INTERACTIONS

none reported to date

CONTRAINDICATIONS

- known hypersensitivity to goserelin
- pregnancy

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days) **EARLY ONSET** (days to weeks)

disease flare (increased bone pain)

4% urinary tract obstruction 1%

spinal cord compression 1%

impotence and/or decreased sex drive; (decreased libido)

hot flushes (60-80%)

nausea and vomiting (1%)

increased alkaline phosphatase (2%)

pain and redness at injection site (4%)

skin rash (including erythema and urticaria, 2%)

breast swelling and/or tenderness

(gynecomastia, 2-3%)

Continued Next Page...

GOSERELIN

CLINICAL MONITORING

RECOMMENDED CRITERIA

NO RECOMMENDED TOXICITY RATINGS

SUGGESTED CRITERIA

- Periodic **liver function tests** (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated))

PHARMACEUTICAL CONSIDERATIONS

Depot injection

3.6 mg or 10.8 mg as goserelin acetate in a sustained release vehicle. In a prefilled, ready-to-use, sterile syringe with 16 gauge needle. The vehicle is a solid cylindrical rod consisting of a matrix of D,L-lactic and glycolic acids copolymer which is biodegradable, biocompatible and non-antigenic. Store syringe in its protective pouch, below 25°C and protected from light and moisture.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level: Take Home
Prescription (NOTE: Use of
preprinted Physician Standing Order
is recommended); Depot
administration in Physician's Office
CDHA Status Formulary
Pharmacare Status Formulary

GRANISETRON

(Antiemetic; Serotonin [5-HT₃]-Receptor Antagonist)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Kytril®

Vial with 1mg/1mL Granisetron

White tablets with 1mg Granisetron

MECHANISM OF ACTION

Selective serotonin receptor (5-HT₃) antagonist, blocking serotonin both peripherally (primary site of action) and centrally at the chemoreceptor trigger zone.

PHARMACOKINETICS

Oral Absorption

yes

Distribution

widely distributed throughout the body.

Excretion in breast-milk unknown.

cross blood brain barrier? No information

Vd- 2-4 L/kg PPB- 65%

Metabolism

Liver, by N-demethylation, aromatic ring oxidation, and conjugation

Excretion

Predominantly hepatic (CYT P450 3A)

The remainder of the dose is excreted as

metabolites, 48% to 49% in the urine,

34% to 38% in the feces

Urine: I V: 12%; oral 11%

t_{1/2} - I V: cancer patients: 10-12 hours,

Normal volunteers: 4-5 hours

oral: Normal volunteers: 6-23 hours

IV COMPATIBILITY

Normal saline, 5% Dextrose

ROUTES

orally

I V: as a rapid push (30 sec) or short (5 to 15 min) bolus infusion

ADMINISTRATION

- Mix in 50mL minibag (5% Dextrose, Normal Saline); Infuse over 15 minutes

EXTRAVASATION HAZARD

no

INDICATIONS AND OTHER USES

- Prevention of nausea & vomiting from emetogenic chemotherapy or radiotherapy

CONTRAINDICATIONS

- pregnancy
- severe liver disease

DOSING

Oral

- 2mg po given 1 hour prior to chemotherapy or radiotherapy; some oncologists prefer to give 1mg po pre-chemo and 1mg po 12 hours later (or qhs for convenience)

Pediatric

Intravenous

- 10 µg/Kg before chemotherapy- children 2-16 years old
- Safety & effectiveness not established for children < 2 yrs old

Injection

- 10µg/Kg or 'flat' dose of 1mg IV, 30 minutes before chemotherapy
- May dilute 1 mg granisetron in 50mL NS or D5W and infuse volume for patient dose over 15 minutes (volume equals 50% body weight- e.g. 80Kg patient given 40mL of diluted solution)
- Granisetron should not be admixed with any other drugs

Other dosing may be indicated

SIGNIFICANT INTERACTIONS

Cytochrome P450 substrates

GRANISETRON

SIDE EFFECTS

* may be life-threatening

side effects in **bold**, *italic* type are common

IMMEDIATE ONSET (hours to days)

EARLY ONSET (days to weeks)

headache (10-21%)

rare: arrhythmias, chest pain,

abdominal pain, constipation, diarrhea

hypersensitivity reaction

CLINICAL MONITORING

RECOMMENDED CRITERIA

SUGGESTED CRITERIA

NO RECOMMENDED TOXICITY
RATINGS

NO ADDITIONAL TOXICITY RATINGS

PHARMACEUTICAL CONSIDERATIONS

Tablets: 1mg triangular white tablets. Store at room temperature.

Injection: Vials with 1mg/1mL clear solution. Preservative-free.

Diluted solution for infusion

Compatible with D5W or NS. May be diluted in 50mL NS or D5W and infused over 15 minutes. Administer volume for patient-specific dose, as illustrated in table:

Patient Weight (Kg)	40	50	60	70	80	90	100
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Volume of diluted solution (1mg/50mL)	20	25	30	35	40	45	50
---------------------------------------	----	----	----	----	----	----	----

Flush IV line before and after dolasetron injection to prevent mixture with other incompatible drugs.

Incompatible with several other drugs, including dexamethasone. Granisetron should not be admixed with any other drugs.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-

Injection-Basic Level;

Oral- Take Home Prescription

Indication restriction- Provincial

Cancer Drug Formulary

CDHA Formulary Status-

Non-Formulary

Pharmacare Formulary Status-

Non-Formulary

HYDROXYUREA

(Antineoplastic Agent, Miscellaneous)

Revision Date: Feb 03

DRUG

COMMERCIAL PRODUCT DESCRIPTION

Brand Name:

Hydrea®

Capsules with 500mg of Hydroxyurea

MECHANISM OF ACTION

Hydroxyurea appears to inhibit DNA synthesis without inhibiting RNA or protein synthesis, by inhibition of ribonucleotide reductase. It may also inhibit incorporation of thymidine into DNA and directly damage DNA. Hydroxyurea is specific for the S phase of the cell cycle, but may also arrest cells in the G1 phase. Blocking the G1-S interface, when sensitivity to radiation is at its maximum, may account for the drug's activity as a radiation sensitizer.

PHARMACOKINETICS

Oral Absorption

readily absorbed from gastrointestinal tract (90%)

Distribution

distributed throughout body, crosses placenta, found in ascitic fluid; enters breast milk

cross blood brain barrier? yes;

peak CSF levels at 3 hours; CSF: plasma ratio 1:4 to 1:2

Vd: 0.5 L/kg PPB: no information

Metabolism

50% metabolized in liver to CO₂ and urea (50%)

metabolite(s): active- no
inactive- carbon dioxide, urea

Excretion

renal: 80% as intact drug (50%), and urea (30%)

50% of a dose recovered in urine within 12 hours, mainly as intact drug. The rest is excreted as carbon dioxide via the lungs or via the urine as urea.

Urine: 80% within 12 hours as intact drug or urea

t_{1/2}: 1-2 hours Cl: no information

CONTRAINDICATIONS

- known hypersensitivity to hydroxyurea, cytarabine, fluorouracil

ANTIEMETIC RISK

LOW RISK (Less than 10% of patients)

- No routine antiemetic pre-chemotherapy or post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

ROUTES

oral

DOSING

CML:

- daily: 1-1.5 g po, adjusted to keep WBC about 20-30 x 10⁹/L
- daily: 20-30 mg/kg po

Solid tumours:

- q3d: 80 mg/kg as a single dose po, starting 7 days prior to radiation therapy

Adequate trial: 6 weeks

Impending leucostasis:

- 1-3 g po loading dose and 0.5-1 g po hourly to reduce WBC count rapidly

Pediatric

CML:

daily: 10-20 mg/kg po, adjusted to hematological response

Brain tumours:

q2-4w: 1.5-3 g/m² po

Other dosing may be indicated

INDICATIONS AND OTHER USES

- Chronic myelogenous leukemia
- Head and neck cancer, squamous cell
- Malignant melanoma
- Ovarian cancer

OTHER ONCOLOGY USES

Acute myelogenous leukemia

Brain tumours, pediatric

Polycythemia rubra vera

Continued Next Page...

HYDROXYUREA

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

allergic reactions (fever, serum sickness)
nausea and vomiting (mild), diarrhea,
loss of appetite (anorexia)
increased uric acid levels
(**hyperuricemia**)
radiation recall reaction (rare)

DELAYED/LATE ONSET (weeks- years)

darkening of skin (hyperpigmentation)
rash

EARLY ONSET (days to weeks)

* **low WBC, RBC, platelets**
(**myelosuppression**, nadir 7 days,
recovery 14-21 days)
anemia (megaloblastosis)
mouth sores (stomatitis)
hair loss (alopecia, rare)
nail changes
reddening of face (facial erythema)
drowsiness
kidney problems (elevated BUN and
creatinine)
increased uric acid levels
(hyperuricemia)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC) and serum uric acid levels** before each cycle of treatment

SUGGESTED CRITERIA

- Baseline and periodic **renal functions tests** [serum creatinine, electrolytes & BUN]
- Periodic **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]

SIGNIFICANT INTERACTIONS

kidney (renal) failure
pregnancy and breast feeding
radiation therapy (synergy), busulfan
(increased effect on leucocyte count)
bone marrow depressants, probenidic,
sulfipyrazone, allopurinaol, colchicine

DOSE ADJUSTMENT CRITERIA

Renal failure: (Suggested action)
Consider dose reduction if renal function
is reduced (eg. If creatinine clearance=
10-50mL/min, reduce to 50% dose; if
CrCl <10mL/min, reduce to 10-20%
dose)

PHARMACEUTICAL CONSIDERATIONS

Capsules

500 mg; store at room temperature;
avoid excessive heat and moisture.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level: Take home
prescription on preprinted Physician
Standing Order
CDHA Status Formulary
Pharmacare Status Formulary
NOTE: It is recommended to limit
ordering of this medication to
preprinted Physician Standing Order
form, for patient safety

IDARUBICIN

(Antineoplastic Agent; Anthracycline, Antibiotic)

Revision Date: Feb 03

DRUG

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Idamycin® Vials with 5mg & 10mg Idarubicin

MECHANISM OF ACTION

Similar to doxorubicin and daunorubicin: inhibition of DNA and RNA synthesis by intercalation between DNA base pairs.

PHARMACOKINETICS

Oral Absorption

rapid but erratic absorption, variable (4% to 77%); mean: about 30% bioavailability

Distribution

bone marrow, extensive tissue uptake and plasma protein binding
cross blood brain barrier? yes
Vd- 64 L/kg (some reports up to 2250 L)
PPB- 94-97%

Metabolism

mainly in liver
metabolite(s) active- idarubicinol
inactive- yes

Excretion

Following I.V. administration, about 16% of the drug is excreted in the urine (3% unchanged, 13% as idarubicinol).
Following oral administration, about 5% of dose is excreted renally (0.5% to 0.7% unchanged, 4% as idarubicinol). About 17% of an I.V. dose and 8% of an oral dose are excreted hepatically.
Urine: 16% (IV) 5% (oral) / 4 days
Feces: 17% (IV) 8% (oral) / 5 days
 $t_{1/2} \alpha$ - 5-30 minutes $t_{1/2} \beta$ - 1-22 hours
 $t_{1/2} \gamma$ - 15-35 hours
oral: 14-35 hours; I.V.: 12-27 hrs
Cl- 122.8 L/hour

IV COMPATIBILITY

normal saline, dextrose 5%, dextrose/saline, lactated Ringers

ROUTES

direct IV (preferred)

ADMINISTRATION

- Slow push through sidearm of free flowing IV (5% Dextrose, Normal Saline). Give over at least 3-5 minutes (administering nurse should be certified to administer IV push chemotherapy agents)
- Slow down injection rate if erythematous streaking occurs

EXTRAVASATION HAZARD

VESICANT (tissue damage on extravasation)
Management- stop IV, aspirate, elevate limb, cold intermittent compresses
Follow Extravasation Guidelines

DOSING

Intravenous:

- q3w: 8 mg/m² IV daily x 5 days
- q3w: 12 mg/m² IV daily x 3 days

Pediatric:

- 8-10 mg/m²/day IV x 3 days

Other dosing may be indicated

INDICATIONS AND OTHER USES

- Acute lymphocytic leukemia
- Acute non-lymphocytic leukemia

OTHER ONCOLOGY USES

Chronic myelogenous leukemia
Non-Hodgkin's lymphoma
Acute myelogenous leukemia
Breast cancer

CONTRAINDICATIONS

- serious heart disease
- previous treatment with cardiotoxic drugs and/or radiation

ANTIEMETIC RISK

HIGH RISK (30-90% of patients)

- Use a serotonin receptor antagonist PLUS dexamethasone pre-chemotherapy and post-chemotherapy
See Nausea & Vomiting Guidelines for more detail

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IDARUBICIN

SIDE EFFECTS

* may be life-threatening

side effects in ***bold, italic*** type are common

IMMEDIATE ONSET (hours to days)

tissue damage on extravasation (vesicant)

flare reaction (histamine release- Symptoms: erythema, pruritus, urticaria, venous streaking)

vein irritation (phlebitis); facial flushing

nausea and vomiting (80%, mild to moderate)

urine discolouration (reddish, lasts 1-2 days)

increased uric acid levels (hyperuricemia)

allergic (skin rash, fever, chills)

irregular heartbeat (rare, transient, acute arrhythmias)

radiation recall reaction (rare)

EARLY ONSET (days to weeks)

* ***low WBC, platelets***
(***myelosuppression*** nadir 6-14 days, recovery 21-24 days)

hair loss (alopecia), usually moderate and partial)

mouth sores (mucositis and esophagitis), starts in 3-10 days)

diarrhea

liver problems (20-30%, increased liver enzymes and bilirubin)

DELAYED/LATE ONSET (weeks- years)

* heart problems (congestive heart failure)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC), serum electrolytes, and serum uric acid levels** before each cycle of treatment
 - Clinical exam for symptoms of **Congestive Heart Failure**
 - Periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels
- CARDIAC**

0. None
1. —
- 2 Asymptomatic, resting ejection fraction decline by >10% baseline; or abnormal cardiac function tests (LVEF >50) with no baseline for comparison
- 3 Mild Congestive Heart Failure, responds to therapy
- 4 Severe/refractory Congestive Heart Failure

At cumulative dose threshold and subsequent intervals

SUGGESTED CRITERIA

- Baseline **liver function tests** (if liver failure suspected) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- Baseline **cardiac function tests** (Echo, RNA and/or MUGA scans) for all patients with cardiac risk factors

For Cardiac Toxicity Ratings:

First rating at the Idarubicin cumulative dose **threshold of 150mg/m²**, & repeat ratings at each cumulative dose **increment of 20mg/m²** above threshold (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation)

Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

IDARUBICIN

PHARMACEUTICAL CONSIDERATIONS

Injection

5 mg, 10 mg vial; contains lactose; store at room temperature (15-30°C), protect from light.

Reconstitute powder with SWI or NS to a final concentration of 1 mg/mL. Do not use bacteriostatic diluents; early experience with doxorubicin suggested that the use of diluents containing benzyl alcohol resulted in hypersensitivity reactions. Vials are under negative pressure.

Reconstituted solution for injection

Clear, orange-red solution. Manufacturer's monograph in Canada states that the reconstituted solution is stable 24 hours at room temperature and 48 hours refrigerated (2-8°C), protected from direct light. However, Trissel's Handbook on Injectable Drugs, 7th Edition, states that the reconstituted solution is physically and chemically stable for 72 hours at room temperature and at least 7 days refrigerated. Like doxorubicin, idarubicin should not be stored in contact with aluminum but may be safely injected through an aluminum-hubbed needle.

Diluted solution for infusion

Compatible in saline, dextrose, dextrose-saline combinations and lactated Ringer's injection for at least 72 hours at room temperature and protected from light. Dilute solutions (10 mg/L) are light sensitive, undergoing some degradation when exposed to light for periods greater than 6 hours; however, the manufacturer does not recommend special precautions to protect freshly prepared solutions for administration.

Some mixtures with amikacin, cimetidine, cyclophosphamide, cytarabine, diphenhydramine, droperidol, erythromycin, magnesium sulfate, mannitol, metoclopramide, potassium chloride, ranitidine and TPN solution are reported to be compatible during simulated Y-site injection. It is recommended that idarubicin not be mixed with other drugs. Incompatible with acyclovir, ampicillin, sulbactam, cefazolin, ceftazidime, clindamycin, dexamethasone, etoposide, furosemide, gentamicin, heparin, hydrocortisone, imipenem-cilastin, lorazepam, meperidine, methotrexate, mezlocillin, sodium bicarbonate, vancomycin and vincristine during simulated Y-site injection. Idarubicin is not stable in alkaline solutions.

SIGNIFICANT INTERACTIONS

previous therapy with other anthracycline agents, other cardiotoxic agents, trastuzumab
myelosuppression-causing agents

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status- Intermediate Level	
CDHA Status	Formulary
Pharmacare Status	Non-Formulary

DOSE ADJUSTMENT CRITERIA

Hepatic dysfunction (*Suggested action*)

1. If Bili= 40-85µmol/L or AST>180IU/L,
REDUCE to **50%** dose
2. If Bili >85µmol/L, **Omit** dose

Renal dysfunction:

If Serum Creatinine >200µmol/L, reduce to **50%** dose



IFOSFAMIDE

(Antineoplastic Agent; Alkylating Agent (Nitrogen Mustard)) *Revision Date: Feb 03*

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Ifex® Vials with 1000mg & 3000mg for reconstitution

MECHANISM OF ACTION

Ifosfamide binds to nucleic acids and intracellular structures, causing cross-linking of DNA strands; inhibits protein and DNA synthesis; it is cell cycle phase nonspecific.

PHARMACOKINETICS

(highly dose-dependent!)

Oral Absorption

100% bioavailability, but associated with significant neurotoxicity

Distribution

largely in body water, limited tissue binding; present in breast milk, present in ascites

cross blood brain barrier?

ifosfamide: yes, but does not reach therapeutic levels

active metabolites: no

Vd- 37-49 L PPB- not appreciably

Metabolism

activated by hepatic microsomal enzyme oxidation system; pathways saturated at higher doses; autoinduction of hepatic metabolism 6 time dependent decrease of half-life

metabolite(s): active- yes:

ifosphoramid mustard, acrolein

inactive- dechloroethylated and carboxy metabolites

Excretion

excreted in kidneys; elimination fits two compartment model for large bolus doses and one compartment model for fractionated doses

urine: 60-80% in 72 hours, 15% as unchanged drug, 41% as metabolites; 31% in children

$t_{1/2}$ - 4 1-15 2 hours; (1800 mg/m²: 4-7 hours; 3800-5000 mg/m²: 11-15 hours)

Cl 60-74 mL/min

ROUTES

intermittent IV (in 75 mL NS over 30-120 minutes, hydrate)

continuous IV (hydrate)

IV COMPATIBILITY

normal saline, dextrose 5%, lactated Ringer's, mesna

ADMINISTRATION

- Bolus dose of Mesna before Ifosfamide infusion; Mesna admixed in Ifosfamide solution, followed by 2 doses of Mesna by IV bolus or PO
 - Short administration: May mix doses ≤ 2000 mg in 100-250mL bag (Normal Saline); Infuse over 30-60 minutes
 - May mix doses > 2000 mg in 500-1000mL bag (Normal Saline); Infuse over 1-4 hours
 - Medium administration: Mix in 1000mL bag (Normal Saline); Infuse over 2-8 hours
 - May be admixed with Mesna solution, when Mesna given by an infusion started before Ifosfamide
 - Longer administration: May be given by continuous infusion over 24-36 hours as inpatient or using ambulatory infusion pump
 - Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration
 - Inadequate total hydration may result in dose-related hemorrhagic cystitis
- Ifosfamide and Mesna Infusion Admixture
- May be diluted in larger volumes for continuous infusion over 6-24 hours; May be infused using an ambulatory infusion pump over longer periods
 - May be infused using an ambulatory infusion pump for periods over 1 day, with a 24 hour supply of solution in each reservoir or IV bag
 - May also be admixed with Cisplatin and/or Etoposide in 1000mL Normal saline, and infused over 1 to 3 hours

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IFOSFAMIDE

EXTRAVASATION HAZARD

local pain, inflammation, induration, phlebitis (1%)

SIGNIFICANT INTERACTIONS

benzodiazepines, clofibrate, CNS depressants (eg. antihistamines, narcotics, antiemetics), dexamethasone, grapefruit (naringenin), phenobarbital, phenytoin, radiation therapy, rifampicin, warfarin, other antineoplastic agents

Cytochrome P450 Substrate

DOSING

Intravenous:

- q3-4w: 50-60 mg/kg/day (2000-2400 mg/m²) x 5 doses (daily or alternate days)
- q3-6w: 1500-2800 mg/m²/day x 4-5 days
- q3-4w: 5000-8000 mg/m² continuous IV over 24 hours
- The use of concurrent mesna is required to prevent severe hematuria from high-dose ifosfamide ≥ 2000 mg/m²/day x 5 days).

Bone marrow transplant:

- much higher doses are used for tumour ablation prior to marrow transplant than for standard treatment regimens; eg. 12,000 mg/m².

Pediatric

Intravenous:

- q3w: 1.8-2.5 g/m²/day x 5 consecutive days
- q3-4w: 3 g/m²/day x 2-3 days

Other dosing may be indicated

DOSE ADJUSTMENT CRITERIA

Hepatic failure: (Suggested action)

Consider dose reduction if LFTs elevated (eg. Bilirubin or AST)

Renal Failure (Suggested action)

1. If Serum Creatinine > 200µmol/L,
REDUCE to **75%** dose
2. If Serum Creatinine > 300µmol/L,
REDUCE to **67%** dose

ANTIEMETIC RISK

HIGH RISK (30-90% of patients)

- Use a serotonin receptor antagonist PLUS dexamethasone pre-chemotherapy and post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

INDICATIONS AND OTHER USES

- Cervical cancer
- Pancreatic cancer
- Sarcoma, soft tissue

OTHER ONCOLOGY USES

Testicular cancer
Brain tumours, pediatric
Breast cancer
Endometrial tumors
Ewing's sarcoma
Gynecologic sarcomas
Hodgkin's disease
Leukemias
Lung cancer
Neuroblastoma
Non-Hodgkin's lymphoma
Osteogenic sarcoma
Ovarian cancer
Rhabdomyosarcoma
Wilm's tumour

CONTRAINDICATIONS

- advanced cerebral arteriosclerosis
- nephrectomy 3 months prior to treatment
- low WBC, RBC, platelets (myelosuppression)
- bladder problems (hemorrhagic cystitis) on treatment

Continued Next Page...

IFOSFAMIDE

SIDE EFFECTS

- * may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

- * anaphylaxis (rare)
- * **nausea and vomiting** (onset few hours, duration 3 days)
- * **bladder problems** (40% without mesna, hematuria, dysuria, frequency, hemorrhagic cystitis)
- vein irritation (chemical phlebitis)

EARLY ONSET (days to weeks)

- * **low WBC, RBC, platelets** (*myelosuppression*, nadir 8-10 days, recovery 14-21 days)
- * **hair loss** (reversible alopecia)
- * **bladder problems** (40% without mesna, hematuria, dysuria, frequency, hemorrhagic cystitis)
- kidney problems (proximal tubular damage, metabolic acidosis, SIADH, syndrome of inappropriate secretion of ADH)
- * heart problems (rare, arrhythmias at high doses)
- * central nervous system problems (encephalopathy, confusion, lethargy, somnolence, seizures, coma)

DELAYED/LATE ONSET (weeks to years)

- kidney problems (proximal tubular damage)
- lung problems (interstitial pneumonitis, rare)
- gonadal damage, sterility

CLINICAL MONITORING

RECOMMENDED CRITERIA

- * **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- * Baseline and periodic **urine output and urinalysis tests (for RBCs)**- Periodic for smaller, daily doses; routinely for larger, single doses
- * Baseline & periodic **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- * Baseline & periodic **renal function tests** [serum creatinine, electrolytes & BUN]
- * Neurologic toxicity ratings (Cortical) at each visit

CYSTITIS

- 0 None
- 1 Mild symptoms
- 2 Symptoms relieved with therapy
- 3 Symptoms not relieved
- 4 Life-threatening

CORTICAL

- 0 None
- 1 Mild somnolence
- 2 Moderate somnolence
- 3 Severe somnolence, confusion, hallucination
- 4 Coma, seizures

Rated At Each Clinic Or Hospital Visit

SUGGESTED CRITERIA

NO ADDITIONAL TOXICITY RATINGS

IFOSFAMIDE

PHARMACEUTICAL CONSIDERATIONS

Injection

1g and 3 g vials; store at room temperature. Temperature above 35°C may cause ifosfamide to liquify without loss of potency.

Reconstitute powder with SWI, benzyl alcohol- or paraben-preserved bacteriostatic water for injection to a final concentration of 50 mg/mL. Higher concentrations in benzyl alcohol-preserved water for injection are reported to be unstable, although an 80 mg/mL solution in preservative-free SWI or NS is stable in a PVC cassette at 37°C for 8 days.

Reconstituted solution for injection

The manufacturer recommends maximum storage of 24 hours at room temperature and 72 hours when refrigerated. Chemically and physically stable for 7 days at 30°C and 3 to 6 weeks refrigerated.

Diluted solution for infusion

Concentrations of 0.6 to 20 mg/mL in D5W, NS and lactated Ringer's are compatible for 7 days at room temperature and 6 weeks when refrigerated. A 7% potency loss was reported after 9 days at 37°C with greater loss at 70°C. The manufacturer recommends maximum storage of 24 hours at room temperature and 72 hours refrigerated, when stored in glass bottles, PVC or PAB (polyolefin) bags.

Stability in syringes

Concentrations of 0.6 and 20 mg/mL in D5W, NS, SWI or lactated Ringer's are chemically stable in polypropylene syringes for at least 24 hours at 30°C. The combination of ifosfamide 50 mg/mL and mesna 40 mg/mL is reported to be stable in a syringe for 7 days at room temperature or refrigerated.

Compatible with ondansetron; also with mesna for at least 24 hours at room temperature in PVC containers. It is recommended that ifosfamide not be mixed with other drugs.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Advanced Level

CDHA Status Formulary

Pharmacare Status Non-Formulary

IMATINIB MESYLATE

(Signal Transduction Inhibitor- Tyrosine Kinase)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Names: Gleevec® Greyish-orange capsules with 100mg of Imatinib free base

Other Name: STI-571

MECHANISM OF ACTION

Imatinib is a protein-tyrosine kinase inhibitor which inhibits tyrosine kinase associated with BCR-ABL. In chronic myeloid leukaemia, the BCR-ABL tyrosine kinase is the abnormal enzyme created by the Philadelphia chromosome. Imatinib inhibits proliferation and induces apoptosis in BCR-ABL positive cells. In vitro, Imatinib also inhibits the receptor tyrosine kinases for platelet-derived growth factor (PDGF), stem cell factor (SCF), c-KIT, and it inhibits PDGF- and SCF-mediated cellular events. Tumours related to c-KIT tyrosine kinase (e.g. gastrointestinal stromal tumours) are also under clinical investigation with Imatinib.

PHARMACOKINETICSOral Absorption

Well-absorbed- mean 98% bioavailability from capsule formulation with C_{max} within 2-4 hours of dose

Distribution

Mean imatinib AUC increased proportionally with increasing dose in the range 25 mg-1000 mg. There was no significant change in the pharmacokinetics of imatinib on repeated dosing, and accumulation is 1.5-2.5 fold at steady state when Gleevec is dosed once daily. PPB- approximately 95%, mostly to albumin and α_2 -acid glycoprotein.

Metabolism

Hepatic metabolism by cytochrome P450 enzymes, mostly CYP3A4. Other cytochrome P450 enzymes (e.g. CYP1A2, CYP2D6, CYP2C9, and CYP2C19) play a minor role in metabolism of Imatinib. Metabolite(s): active- N-demethylated piperazine derivative.

Excretion

predominately in the feces, mostly as metabolites.

Feces: 68% of dose eliminated within 7 days.

Urine: 13% of dose eliminated within 7 days.

$t_{1/2}$: the elimination half-lives of imatinib and its major active metabolite, the N-desmethyl derivative, were approximately 18 and 40 hours, respectively.

CI- 50-year-old patient weighing 50 kg: 8 L/h. 50-year-old patient weighing 100 kg: 14 L/h. Inter-patient variability of 40% in clearance.

ROUTES

Oral

ADMINISTRATION

- Imatinib is sometimes associated with GI irritation. Imatinib should be taken with food and a large glass of water to minimize this problem.
- Therapy should be initiated by a physician experienced in the treatment of patients with chronic myeloid leukemia.

CONTRAINDICATIONS

- patients with hypersensitivity to Imatinib or to any other component of Gleevec.
- women of childbearing potential should be advised to avoid becoming pregnant.

INDICATIONS AND OTHER USES

- Chronic myelogenous leukemia
- OTHER ONCOLOGY USES (Not Approved)

Gastrointestinal Stromal Tumour (GIST)

Acute Lymphocytic Leukemia with Philadelphia chromosome cytogenetics (9:22 translocation)

Continued Next Page

IMATINIB MESYLATE

SIDE EFFECTS

* may be life-threatening

side effects in **bold**, *italic type* are common

IMMEDIATE ONSET (hours to days)
headache (24-28%)
musculoskeletal pain (27-39%)

DELAYED ONSET (weeks- months)
potential toxicities suggested by animal studies
liver toxicity
kidney toxicity
immunosuppression

EARLY ONSET (days to weeks)
* *neutropenia* (16-25%) and *thrombocytopenia* (16-30%), mean duration 2 to 4 weeks
nausea (55-68%) & *vomiting* (28-54%)
muscle cramps (25-46%)
edema (51-66%, most frequently periorbital or in lower limbs)
diarrhea (33-49%)
skin rash (32-39%)
fatigue (24-33%)
* severe edema (1%-5%)
severe elevation of transaminases or bilirubin (1 1%-3 5%)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Baseline & periodic liver function tests [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- Check for edema at each visit

SUGGESTED CRITERIA

- Toxicity ratings of Lethargy and Edema at treatment review visit

LETHARGY

- 0 None
- 1 Mild (Performance Status [PS] decreased by 1)
- 2 Moderate (PS decreased by 2)
- 3 Severe (PS decreased by 3)

EDEMA

- 0 None
- 1 1+ or dependant evening only
- 2 2+ or dependant throughout the day
- 3 3+
- 4 4+ generalized anasarca

SIGNIFICANT INTERACTIONS

Drugs that may **increase** Imatinib plasma concentrations: **CYP3A4 Inhibitors** (e.g. ketoconazole, itraconazole, erythromycin, clarithromycin); Imatinib co-administered with a single dose of ketoconazole- significant increase in exposure to imatinib (mean Cmax and AUC increased by 26% and 40%, respectively)

Drugs that may have their plasma concentration **altered** by Imatinib: **CYP3A4 Substrates** (e.g. simvastatin, warfarin, cyclosporine or pimozide): Imatinib increased the mean C max and AUC of simvastatin (CYP3A4 substrate) by 2- and 3 5- fold, respectively, indicating an inhibition of CYP3A4 by imatinib.

Drugs that may **decrease** Imatinib plasma concentrations: **CYP3A4 Inducers** (e.g., dexamethasone, phenytoin, carbamazepine, rifampicin, phenobarbital or St. John's Wort); Induction of CYP3A4 by phenytoin decreased Imatinib AUC.

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IMATINIB MESYLATE**DOSE ADJUSTMENT CRITERIA**Hepatic dysfunction

If bilirubin $>3 \times$ institutional upper limit of normal (IULN) or liver transaminases $>5 \times$ IULN, **HOLD Imatinib** until bilirubin levels have returned to a $<1.5 \times$ IULN and transaminase levels to $<2.5 \times$ IULN. Treatment may then be continued at a **reduced daily dose** (i.e., 400 mg - 300 mg or 600 mg - 400 mg).

Neutropenia and Thrombocytopenia:

Chronic Phase CML (starting dose 400 mg)

- If ANC $<1.0 \times 10^9$ /L and/or Platelets $<50 \times 10^9$ /L,
 - 1 **Stop Imatinib** until ANC $=1.5 \times 10^9$ /L and Platelets $<50 \times 10^9$ /L platelets $=75 \times 10^9$ /L
 - 2 **Resume treatment with Imatinib at dose of 400 mg**
 - 3 If recurrence of ANC $<1.0 \times 10^9$ /L and/or platelets $<50 \times 10^9$ /L, repeat step 1 and **resume Imatinib at reduced dose of 300 mg**

Accelerated Phase CML and Blast Crisis (starting dose 600 mg)

- If ANC $<0.5 \times 10^9$ /L and/or Platelets $<10 \times 10^9$ /L,
 - 1 Check if cytopenia is related to leukemia (marrow aspirate or biopsy)
 - 2 If cytopenia is unrelated to leukemia, **reduce dose of Imatinib to 400 mg**
 - 3 If cytopenia persist 2 weeks, **reduce further to 300 mg**
 - 4 If cytopenia persist 4 weeks and is still unrelated to leukemia, **stop Imatinib** until ANC $=1 \times 10^9$ /L and platelets $=20 \times 10^9$ /L and then **resume treatment at 300 mg**

GUIDELINES

Visit the **Cancer Care Nova Scotia** website (www.cancercare.ns.ca) for the guideline on Imatinib for chronic myelogenous leukemia

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level; Prescription
ordered on preprinted Physician
Standing Order; *Indication
restriction*- Provincial Cancer Drug
Formulary

CDHA Formulary Status -
Non-Formulary

Pharmacare Formulary Status-
Non-Formulary (Prescriber must
write letter of request for coverage)

NOTE: It is recommended to limit
ordering of this medication to
preprinted Physician Standing Order
form, for patient safety

INTERFERON ALFA

(Antineoplastic Agent, Miscellaneous, Biological Response Modulator: Interferon)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

- Brand Names:** Roferon-A® Vials with 3, 6, 9 or 18 x 10⁶ IU Lyophilized powder or reconstitution of Interferon Alfa 2A
- Intron A®** Vials with 3, 5, 10, or 18 x 10⁶ IU Lyophilized powder for reconstitution of Interferon Alfa 2B. Vials with 3 x 10⁶ IU/0.5 mL, 18 x 10⁶ IU/3 mL, 5 x 10⁶ IU/0.5 mL, 10 x 10⁶ IU/1 mL, 25 x 10⁶ IU/2.5 mL human serum albumin-free solution of Interferon Alfa 2B
- Wellferon®** Vials with 3 x 10⁶ IU/0.5 mL of Interferon Alpha-n1
- Keep under refrigeration

MECHANISM OF ACTION

The exact mechanism of interferon- α 's cytotoxic effect is not clear. The antineoplastic effect does not appear to be linked to interferon's antiviral effect. Possible mechanisms by which interferons stimulate existing host defenses against malignancies include induction of gene transcription, inhibition of cell growth, alteration of cellular differentiation, interference with oncogene expression, and augmentation of lymphocyte toxicity. It also has been shown to increase activation of prenatally killer cells, cytotoxic activity of natural killer cells, macrophage phagocytosis, cytotoxicity of K cells and polymorphonuclear leukocytes, and alter antibody production.

PHARMACOKINETICS

Oral Absorption

rapid but erratic absorption, about 30% bioavailability

Distribution

bone marrow: extensive tissue uptake and plasma protein binding
cross blood brain barrier? no
Vd- 31 L (370-720 L in leukemia patients)

Metabolism

catabolized by proteolysis in renal tubular cells during reabsorption and hepatic metabolism

metabolite(s) active- no inactive- yes

Excretion

renal, some hepatic and biliary disposition described by two-compartment model with an initial distributive t_{1/2} of 7 minutes

urine: no

t_{1/2} α - 7 minutes t_{1/2} β - 2-5 hours

Cl 2.79 mL/min/kg

IV COMPATIBILITY

normal saline, Ringer's, lactated Ringer's, sodium bicarbonate 5%, amino acids

NOT stable in D5W

ROUTES

- subcutaneous (preferred, rotate sites)
- intramuscular (rotate sites)
- direct IV (over 3-5 minutes)
- intermittent IV (over 30 minutes)
- intraperitoneal (final volume 2 L, dwell time 24 hours)
- intravesical (in 60-100 mL, dwell time 24 hours)

ADMINISTRATION

- Subcutaneous self-administration (or administered by home caregiver)
- Reconstitute powder (do not use ready-to-use solution), mix in 100mL bag of Normal Saline; Infuse over 20-30 minutes
- Monitor blood pressure during infusion

EXTRAVASATION HAZARD

none

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INTERFERON ALFA

DOSING

Intravenous:

weekly:

- 3 MU SC/IM for one dose on days 1, 3 and 5 (total dose per cycle 90 MU)
- 3-10 MU/m² (range 2-30 MU/m²) SC/IM for one dose on days 1, 3 and 5 (total dose per cycle 9-30 MU/m² [range 6-90 MU/m²])

daily:

- 3-36 MU SC/IM
- 5 MU/m² (range 3-30 MU/m²) SC/IM

weekly:

- 20 MU/m² IV once daily for 5 consecutive days starting on day 1 for 4 weeks.
- Follow by 10 MU/m² SC for one dose on days 1, 3 and 5 for 48 weeks.

Adequate trial:

- basal cell carcinoma: 8-12 weeks
- hairy cell leukemia: 6 months
- Kaposi's sarcoma: 4-12 weeks

Intralesional:

weekly:

- 1.5 MU/0.15 mL intralesional injection for one dose on days 1, 3 and 5 (total dose per cycle 4.5 MU)

usual total duration of therapy is 3 weeks (ie, 13.5 MU/lesion) (maximum of 3 lesions at one time)

Pediatric: 1 MU/m²/day SC, increase as tolerated to 3 MU/m²/day

Other dosing may be indicated in specific regimens

SIDE EFFECTS

* may be life-threatening

side effects in **bold**, *italic* type are common

IMMEDIATE ONSET (hours to days)

- * allergic reaction (hypersensitivity, rare)
- * irregular heartbeat (arrhythmias, hypotension, 14%, severe 3%)
- flu-like symptoms** (fever, fatigue, chills, 46-68%)
- nausea (21-28%, severe 1%), vomiting (6-14%, severe 1%)
- injection site problems (20%)
- altered sensations (paresthesias, 6%)

EARLY ONSET (days to weeks)

- * low WBC, RBC, **platelets** (myelosuppression, nadir 17-22 days)
- diarrhea (18-45%)
- loss of appetite (anorexia)
- nausea and vomiting
- liver problems** (elevated liver function tests)
- hair loss (uncommon, reversible alopecia)
- rash (transient)
- central nervous system problems (usually reversible, confusion, depression, headache (6-28%), seizures (rare))
- problems with vision (7%)

INTERFERON ALFA

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes before each cycle of treatment
- Routine toxicity ratings of Flu-like Symptoms, Lethargy at follow-up visits

SUGGESTED CRITERIA

- Periodic blood pressure tests
- Periodic liver function tests [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- Baseline chest X-ray & electrocardiogram (EKG)
- Baseline cardiac function tests (Echo, RNA and/or MUGA scans) for all patients with cardiac risk factors

LETHARGY

- 0 None
- 1 Mild (Performance Status decreased by 1)
- 2 Moderate (Performance Status decreased by 2)
- 3 Severe (Performance Status decreased by 3)

FLU-LIKE SYMPTOMS

- 0 None
- 1 Mild
- 2 Moderate
- 3 Severe

(Arthralgia, myalgia, diaphoresis, rigours/chills)

Rated At Monthly/quarterly Clinic Visit

INDICATIONS AND OTHER USES

- Chronic myelogenous leukemia
- Hairy cell leukemia
- Hemangiomas of infancy and childhood
- Kaposi's sarcoma
- Malignant melanoma

OTHER ONCOLOGY USES

Basal cell carcinoma

Bladder cancer

Multiple myeloma

Mycosis fungoides

Non-Hodgkin's lymphoma

Renal cell carcinoma

SIGNIFICANT INTERACTIONS

- ACE Inhibitors (e.g. captopril)
- Cimetidine
- Melphalan, Vinblastine
- Corticosteroids
- Theophylline
- Warfarin
- Zidovudine

GUIDELINES

Visit the **Cancer Care Nova Scotia** website (www.cancercare.ns.ca) for the guideline on Interferon for renal cell cancer

CONTRAINDICATIONS

- low WBC, RBC, platelets (myelosuppression)
- pre-existing psychiatric disorder (or significant history)
- autoimmune hepatitis or history of autoimmune disease

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-

Intravenous (high dose):

Advanced Level; **Subcutaneous** (low dose): Basic Level

Community Level for Take Home Prescription ordered on Physician Standing Order

Indication restriction- Provincial Cancer Drug Formulary

CDHA Status Formulary- Restricted Pharmacare Status Formulary (red); Exception Status

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INTERFERON ALFA

PHARMACEUTICAL CONSIDERATIONS

Swirl all powders gently to reconstitute; do not shake as vigorous shaking may damage the protein.

Only Intron A® (interferon alfa-2b) is HPB approved for intravenous administration. Intron-A® Injection, powder vials of 10 million and 18 million units (MU), contains human albumin. Store in refrigerator. Stable at room temperature for 4 weeks. One reference (Dalton-Bunnow) states that Intron-A may be stored for 24 hours at 45° C and for 1 month at 25° C while another (Sterchele) states a stability of 18 months at room temperature.

Ready-to-use solution of 6 MU/mL (3 MU, 18 MU vials) and 10 MU/mL (5 MU, 10 MU, 25 MU vials); store in refrigerator. Stable at room temperature for 7 days; vials can be put back in the refrigerator at any time during this 7-day period. Any unused solution is stable refrigerated for 7 days.

Multi-dose pen of 15 MU/mL (18 MU pen), 25 MU/mL (30 MU pen) and 50 MU/mL (60 MU pen); store in refrigerator. Stable at room temperature for a total of 48 hours of exposure over a 2-week period.

Reconstitute Intron-A® powder with 1 mL SWI or BWI to yield interferon concentration of 10 MU/mL (10 MU vial) or 18 MU/mL (18 MU vial). A 1 mL vial of BWI is provided.

Reconstituted Intron-A® solution for injection: Clear, colourless to light yellow solution. Physically stable at room temperature for 2 weeks or for 1 month refrigerated when reconstituted with BWI. Physically stable at room temperature or refrigerated for 24 hours when reconstituted with SWI. Schering reports an in-house compatibility study (Feb 17, 1993) which found the 10 MU/mL solution stable for four weeks in polypropylene tuberculin syringes (BD Plastipak) when stored frozen at below -10° C. An additional freeze-thaw-freeze cycle did not affect the stability. Roferon-A® Injection: 3 MU, 4.5 MU, 9 MU and 18 MU vials powder. Powders contain human serum albumin 5 mg per vial. Store powders below 25° C. Also available as 3 MU/mL (1 mL vial), 6 MU/mL (3 mL vial) and 36 MU/mL (1 mL vial) solutions. Each mL of solution contains human serum albumin 5 mg, phenol 3 mg as preservative, and sodium hydroxide or hydrochloric acid to adjust pH. Store solutions in refrigerator. Do not freeze or shake.

Reconstitute Roferon-A® powders with 1 mL SWI; concentration based on vial size.

Reconstituted Roferon-A® solution for injection: Powders reconstituted with SWI should be stored below 25° C and used within 2 hours, or within 24 hours if stored in the refrigerator. Ready-to-use solutions should be stored in the refrigerator and partial vials used within 30 days; protect all solutions from freezing.

Diluted solution for infusion: Compatible with NS, Ringer's solution, lactated Ringer's solution, amino acid solutions, sodium bicarbonate 5% solution. Not compatible with D5W. Prepare immediately before use.

Reconstituted Intron-A® solution for injection can be further diluted with 100 mL NS in glass bottles or PVC bags. The final concentrations should be between 0.05 MU/mL (ie, 50,000 units/mL) to 1 MU/mL; diluted solution is stable at room temperature or refrigerated for 24 hours.

Ready-to-use Intron-A® solution can be further diluted with 50 mL NS in glass bottles or PVC bags. The final concentrations should be no less than 0.3 MU/mL; diluted solution is stable at room temperature or refrigerated for 24 hours.

It is recommended that interferon not be mixed with other drugs.

IRINOTECAN

(Antineoplastic Agent; Topoisomerase Inhibitor)

Revision Date: Feb 03

DRUG

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Camptosar®

Vials with 20mg/0.5mL & 80mg/2mL

Other Name: CPT-11

Irinotecan (pale yellow solution)

MECHANISM OF ACTION

Irinotecan is a semisynthetic derivative of camptothecin that inhibits topoisomerase 1. Inhibition of topoisomerase 1 leads to arrest of DNA replication and ultimately to cell death.

PHARMACOKINETICS

Oral Absorption

no information

Distribution

enters breast-milk

cross blood brain barrier? No information

Vd- 110L/m² PPB- Irinotecan- 30-

68%; SN-38: 95%

Metabolism

primarily hepatic, via carboxylase-mediated cleavage of carbamate bond metabolite(s): active- SN-38 metabolite, SN-38 glucuronide

Excretion

renal- 11-20% as unchanged irinotecan;

0.1% as SN-38; 1-3% as SN-38

glucuronide

Urine: yes

t_{1/2} α - 5.8 hrs (irinotecan)

t_{1/2} β - 10.4 hours (SN-38)

Cl- 13.3 +/- 6.0 L/hrs/m² total systemic clearance

IV COMPATIBILITY

dextrose 5% stable 48hrs at 2-8 °C.

24 hours at room temperature

sodium chloride 0.9% stable 24hrs at room temperature

ROUTES

intravenous infusion over 90 minutes

ADMINISTRATION

- Mix in 500mL bag (5% Dextrose). Infuse over 90 minutes
- Monitor for symptoms of acute cholinergic symptoms; administer Atropine 0.25-1.0mg SC to treat symptoms, repeat as necessary
- Consider premedication with 0.25-1.0 mg atropine subcutaneously for subsequent doses
- Infusion rate may influence the incidence of cholinergic effects
- Protect from light

EXTRAVASATION HAZARD

- Infusion site monitored for signs of inflammation. If extravasation occurs flushing the site with sterile water and/or applying ice to the area are recommended

ANTIEMETIC RISK

HIGH RISK (30-90% of patients)

- Use a serotonin receptor antagonist PLUS dexamethasone pre-chemotherapy and post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

SIGNIFICANT INTERACTIONS

dexamethasone, prochlorperazine, myelosuppressive agents, laxatives, diuretics

DOSING

Intravenous:

Other dosing may be indicated

3 weeks:

- 350 mg/m² (range 200-350 mg/m²) IV for one dose on day 1
- maximum single dose: 700 mg

4 weeks:

- 60 mg/m² IV for one dose on days 1, 8 and 15
- (total dose per cycle 180 mg/m²)

6 weeks:

- 125 mg/m² (range 50-150 mg/m²) IV for one dose on days 1, 8, 15 and 22
- (total dose per cycle 500 mg/m² [range 200-600 mg/m²])

NB, sometimes referred to as the "weekly schedule"

Pediatric: No pediatric indications

IRINOTECAN

SIDE EFFECTS

* may be life-threatening

side effects in **bold**, *italic* type are common

IMMEDIATE ONSET (hours to days) **EARLY ONSET** (days to weeks)

* **diarrhea**

acute cholinergic effects (during the infusion and within 24 hours of the infusion- Symptoms: abdominal cramping, diarrhea, diaphoresis, flushing, rhinitis, increased salivation and lacrimation)

nausea & vomiting

* **diarrhea**

* **myelosuppression**
alopecia

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count** including **differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- Routine assessment of **Diarrhea**, at each clinic visit and telephone reinforcement

DIARRHEA

0. None

1. Increase of 2-3 stools/day over pretreatment
2. Increase of 4-6 stools/day or nocturnal stools
3. Increase of 7-9 stools/day, incontinence, malabsorption
4. Increase of ≥ 10 stools/day, grossly bloody diarrhea, need for parenteral nutrition support

Rated at each visit and between visits by telephone assessment

SUGGESTED CRITERIA

NO ADDITIONAL TOXICITY RATINGS

INDICATIONS AND OTHER USES

- Colorectal cancer

OTHER ONCOLOGY USES

Cervical cancer
Esophageal cancer
Gastric cancer
Glioma
Lung cancer
Mesothelioma
Pancreatic cancer

CONTRAINDICATIONS

- pregnancy (potential harm to fetus)
- hepatic dysfunction (i.e., elevated bilirubin)

DOSE ADJUSTMENT CRITERIA

Diarrhea

- If grade 2, **reduce Irinotecan by 25mg/m²**
- If grade 3, **HOLD** until $\leq$ grade 2, then **restart at dose reduced by 25mg/m²**
- If grade 4, **HOLD** until $\leq$ grade 2, then **restart at dose reduced by 50mg/m²**

Hepatic Dysfunction:

Consider dose reduction if modestly elevated bilirubin (17-35 μ mol/L) in patients with prior pelvic/abdominal radiation

- No information in patients with elevated bilirubin ($>35\mu$ mol/L) or transaminases $>3\times$ ULN (upper limit of normal)

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IRINOTECAN

PHARMACEUTICAL CONSIDERATIONS

Injection: 40 mg and 100 mg vials; each mL contains 20 mg irinotecan hydrochloride trihydrate. Store at room temperature. Protect from light. For single use only, unused portions must be discarded. Freezing irinotecan and admixtures may result in precipitation of the drug and should be avoided.

Diluted solution for infusion: Must be diluted prior to infusion, using D5W (preferred) or NS, to a final concentration range of 0.12-1.1 mg/mL. Physically and chemically stable for up to 24 hours at room temperature and in ambient fluorescent lighting; manufacturer recommends use within 6 hours. Solutions diluted in D5W and stored at refrigerated temperatures and protected from light are physically and chemically stable for 48 hours; manufacturer recommends use within 24 hours. Refrigeration of admixtures using NS is not recommended due to a low and sporadic incidence of visible particulates. In most clinical trials, the irinotecan dose was diluted in 250-500 mL D5W.

Compatibility: It is recommended that irinotecan not be mixed with other drugs.

Treatment of acute cholinergic syndrome: Stop the infusion and administer 0.25 mg of atropine subcutaneously as per physician's order and page the physician. If symptoms are persistent, a repeat dose (0.25-1.0 mg) of atropine subcutaneously as per physician's instructions may be required (monitor pulse for bradycardia). Consider premedication with 0.25-1.0 mg atropine subcutaneously for subsequent doses.

To prevent late onset diarrhea (occurring more than 24 hours after irinotecan administration), instruct patients to take loperamide 4 mg at the first sign of any change in bowel movement (i.e. poorly formed stools or more frequent bowel movements - deviation from normal pattern), then take 2 mg every two hours until diarrhea free for 12 hours. Loperamide may be given as 4 mg every four hours at night instead of 2 mg every 2 hours. Avoid laxative use if possible. There is no daily maximum dose of loperamide.

If laxatives must be used, caution should be taken during irinotecan therapy as this may worsen the incidence or severity of diarrhea.

The use of diuretics should be carefully monitored due to the potential risk of dehydration secondary to possible vomiting and/or diarrhea.

GUIDELINES

Visit the **Cancer Care Nova Scotia** website (www.cancercare.ns.ca) for the guideline on Irinotecan for colorectal cancer

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Intermediate Level; *Indication
restriction-* Provincial Cancer Drug
Formulary
CDHA Formulary Status- Formulary-
Restricted
Pharmacare Formulary Status-
Non-Formulary

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Femara® Dark yellow tablets with 2.5mg Letrozole

MECHANISM OF ACTION

Inhibits the aromatase enzyme responsible for conversion of androstenedione to estrone and testosterone to estradiol, resulting in reduction of plasma estrogen levels.

PHARMACOKINETICS

Oral Absorption

rapidly and completely; not affected by food

Distribution

rapidly and extensively into tissues, excretion in breast-milk unknown

Vd- 1.9L/Kg PPB- 60%, mainly to albumin

Metabolism

hepatic CYT P450 3A4 and 2A6 to an inactive carbinol metabolite and ketone analog

metabolite(s): inactive- yes, carbinol metabolite

Excretion

Hepatic metabolism (~85%) and renal excretion (~11%)

Urine: yes, about 5% as unchanged drug

t½ 2 days

ROUTES

oral

DOSING

Oral:

- 2.5 mg PO once daily.
- Administer with food or on empty stomach.

Pediatric: No pediatric indications

Other dosing may be indicated

INDICATIONS AND OTHER USES

- Breast cancer

CONTRAINDICATIONS

- pregnancy, lactation
- premenopausal endocrine status

SIGNIFICANT INTERACTIONS

tamoxifen

Cytochrome P450 3A Substrate & 2D6, 2A6 & 2C19inhibitor

SIDE EFFECTS

* may be life-threatening

side effects in **bold**, *italic* type are common

IMMEDIATE ONSET (hours to days) **DELAYED/LATE ONSET**

nausea

asthenia

diarrhea

back pain

EARLY ONSET (days to weeks)

hot flushes, vaginal dryness

headache

CLINICAL MONITORING

RECOMMENDED CRITERIA

SUGGESTED CRITERIA

NO RECOMMENDED TOXICITY RATINGS

NO ADDITIONAL TOXICITY RATINGS

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status- Community Level

Take Home Prescription (NOTE: Use of preprinted Physician Standing Order is recommended)

CDHA Status Non-Formulary

Pharmacare Status Formulary

(Antidote, Methotrexate; Folic Acid Derivative)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Leucovorin

Vials with 50mg/5mL, 500mg/50mL

Generic products available

Tablets with 5mg & 15mg Leucovorin

MECHANISM OF ACTION

Leucovorin is a reduced form of folic acid. Reduced folates function as 1 carbon donors in the synthesis of thymidine and purines for DNA, RNA, and proteins. When given following folic acid antagonists, leucovorin bypasses the inhibition of dihydrofolate reductase induced by the antagonist. This allows for recovery of normal tissues, hopefully after irreversible toxicity to tumour tissue has occurred. When given before/with 5-FU, leucovorin provides the folate cofactors that stabilize the binding of 5-dUMP (active nucleotide of 5-FU) and thymidylate synthase. This enhances the activity of 5-FU.

PHARMACOKINETICSOral Absorption

Commercially available leucovorin consists of equal amounts of L- and D-isomers. The L-isomer is preferentially absorbed: 98% at doses of 25 mg decreasing to 31% after a single dose of 200mg

Distribution

distributed to all tissues, present in ascitic fluid, enters breast-milk
cross blood brain barrier? yes
Vd- 3.2 L/kg PPB- 35-45%

Metabolism

After oral administration: L-isomer: rapidly and extensively converted to 5-methyltetrahydrofolate by GI mucosa and in the liver.

After parenteral administration: L-isomer: extensively metabolized to 5-methyltetrahydrofolate and other reduced folate cofactors

D-isomer: excreted unchanged in the urine.

metabolite(s): inactive- Yes
active- 5-methyltetrahydrofolate

Excretion

rapidly eliminated in urine; 5-methylhydrofolate is cleared by both renal and hepatic mechanisms

Urine: 80-90% of dose

t_{1/2} L-isomer: 30-40 min; D-isomer: 7-8 hours, 5-methyltetrahydrofolate: 3 hours

Cl- 3.9 mL/min/kg

IV COMPATIBILITY

normal saline, dextrose 5%, dextrose 10%, Ringer's, lactated Ringer's

ROUTES

oral

intramuscular (rotate sites, deltoid preferred)

direct IV (maximum rate 160 mg/minute)

intermittent IV (maximum rate 160 mg/minute)

ADMINISTRATION

- Doses ≤ 100 mg may be given by push through sidearm of free flowing IV (5% Dextrose, Normal Saline), the injection must not exceed 160mg/min of leucovorin (due to calcium content) (*administering nurse should be certified to administer IV push chemotherapy agents*)
- May be given by direct IV push, followed by a Normal Saline flush, if no IV line has been set up
- May be mixed in 50mL minibag (doses >100mg) or 100mL minibag (doses >500mg) (Normal Saline, 5% Dextrose); Infuse over 15-30 minutes

EXTRAVASATION HAZARD

none

Continued Next Page...

LEUCOVORIN

DOSING

With fluorouracil:

- q4w. 20-200 mg/m² IV x 5 days

Rescue after methotrexate:

- Administer within 24-36 hours. Because absorption is saturable, doses >25 mg should be given IV.

Moderate-dose methotrexate (eg, 350 mg/m², 3000 mg/m²):

- 15-25 mg po q6h x 6-12 doses, starting 24 hours after methotrexate

High-dose methotrexate (eg, 10 g/m²):

- Adjust Leucovorin dose if Methotrexate (MTX) levels elevated

Leucovorin Dose Adjustment (QEII Physician Standing Orders):

24 hour MTX level	48 hour MTX level	72 hour MTX level	Leucovorin Dose/ Interval
≤10 µmol/L	≤1 µmol/L	≤0.5 µmol/L	20mg q6h IV
>10-50 µmol/L	>1-5 µmol/L	0.5-5 µmol/L	20mg q3h IV
>50-500 µmol/L	5-100 µmol/L	5-50 µmol/L	150mg q3h IV
>500 µmol/L	>100 µmol/L	>50 µmol/L	1000mg q3h IV

Note: There are other approaches to pharmacokinetic monitoring after high-dose methotrexate. Consult with the prescriber to determine which program is being followed. Another dose adjustment schema is below.

- 12 mg/m² po q6h x 12 doses, starting 24 hours after the start of the methotrexate infusion
- Modified rescue doses for methotrexate levels >5 x 10⁻⁶ M at 48 hours from start of methotrexate infusion (based on the nomogram of Bleyer 1977):

methotrexate level	leucovorin dose	Other dosing may be indicated in specific regimens
<1 x 10 ⁻⁶ M	12 mg/m ² q6h	
<8 x 10 ⁻⁶ M	100 mg/m ² q6h	
>8 x 10 ⁻⁶ M	1000 mg/m ² q6h	

- Repeat methotrexate levels every 24 hours and adjust leucovorin dose until methotrexate level is <5 x 10⁻⁸ M.
- High dose leucovorin should be limited to high-risk patients (ie, those with elevated methotrexate levels as above 48 hours from start of methotrexate) as progressive increases in leucovorin may compromise the antitumour effect.

Pediatric

- 10 mg/m²/dose po/IV q6h x 72 hours, beginning within 24 hours of methotrexate administration
- *Rescue for high-dose methotrexate:* same doses as for adults

SIDE EFFECTS

- * may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

- allergic (rare)
- diarrhea (when used with fluorouracil)
- mouth sores (stomatitis when used with fluorouracil)

EARLY ONSET (days to weeks)

- diarrhea (when used with fluorouracil)
- mouth sores (stomatitis when used with fluorouracil)
- low WBC, RBC, platelets (myelosuppression, when used with fluorouracil)

Continued Next Page

LEUCOVORIN

CLINICAL MONITORING

RECOMMENDED CRITERIA

No Recommended Toxicity Ratings

SUGGESTED CRITERIA

No Additional Toxicity Ratings

INDICATIONS AND OTHER USES

- Leucovorin rescue after methotrexate (eg. $>300 \text{ mg/m}^2$)
- Acute lymphocytic leukemia
- Breast cancer
- Head and neck cancer, squamous cell
- Non-Hodgkin's lymphoma
- Osteogenic sarcoma
- Enhance cytotoxicity of fluorouracil. Colorectal cancer, other cancers

OTHER ONCOLOGY USES

Choriocarcinoma

Lung cancer, non-small cell

Rhabdomyosarcoma

Breast cancer

CONTRAINDICATIONS

- known hypersensitivity to leucovorin

SIGNIFICANT INTERACTIONS

methotrexate, *fluorouracil

*enhanced cytotoxicity- may be used for therapeutic endpoint

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-

Injection-Basic Level

Oral- Take Home Prescription

CDHA Status

Formulary

Pharmacare Status

Formulary

PHARMACEUTICAL CONSIDERATIONS

Tablets. 5 mg, each mg of drug contains 0.004 mEq calcium, tartrazine-free, store at room temperature (15-30°C).

Injection

50 mg vial, 350 mg vial, 10 mg/mL (5 mL vial, 35 mL vial, 50 mL vial, preservative-free). Store powders at room temperature, refrigerate solutions, protect from light. Each mg of drug contains 0.004 mEq calcium.

Reconstitute powder with SWI. BWI may be used to reconstitute for IM use but, because of its benzyl alcohol content, BWI is not recommended for reconstitution of large doses ($>10 \text{ mg/m}^2$) for IV use. The 50 mg vial may be reconstituted with 2 or 10 mL to a final concentration of 25 or 5 mg/mL respectively. The 350 mg vial may be reconstituted with 17.5 or 35 mL to a final concentration of 20 or 10 mg/mL respectively.

Reconstituted solution for injection

Reconstituted solution is chemically stable for 7 days at room temperature and protected from light. When reconstituted with SWI, it is recommended that the solution be used immediately because of the possibility of microbial contamination. Solutions reconstituted with BWI should be used within 24 hours if stored at room temperature and within 72 hours if stored in the refrigerator. One manufacturer (DBL) reports that leucovorin 10 mg/mL, stored at 9°C in plastic syringes, is stable for 7 days.

Diluted solution for infusion

Solutions of 0.05 mg/mL have shown stability in D5W, D10W, D10NS, NS, Ringer's and lactated Ringer's for at least 24 hours at room temperature and protected from light. One manufacturer (DBL) recommends that dilutions in hypertonic solutions (D10W, D5NS) be discarded after 8 hours.

Physically compatible with cisplatin and fluorouracil at certain concentrations for up to 15 days at room temperature, protected from light. It is recommended that leucovorin not be mixed with other drugs. Incompatible with droperidol and foscarnet.



LEUPROLIDE

(Hormone (Gonadotropin Hormone-Releasing Hormone) Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Lupron®

Multidose vials with 2.8 mL of 5 mg/mL Leuprolide and 14 day injection kit

Lupron Depot®

Prefilled syringes with 7.5 mg, 22.5 mg or 30 mg

MECHANISM OF ACTION

Leuprolide is a synthetic analog of luteinizing-hormone-releasing hormone (LHRH). Following an initial stimulation of luteinizing hormone (LH) and follicle stimulating hormone (FSH) release, chronic administration results in a sustained suppression of LH and FSH release. Serum testosterone falls to levels comparable to surgical castration. It may also have a direct inhibitory effect on the testes, or act by a different mechanism not directly related to reduction in serum testosterone.

PHARMACOKINETICS

Oral Absorption

destroyed in gastrointestinal tract

Distribution

undetermined, like natural GnRH depot injection provides plasma concentrations over a period of one month, excretion in breast-milk unknown

cross blood brain barrier? no information

Vd- Male: 27 L PPB- 43% to 48%

Metabolism

extensive, to amino acids, sites unknown
metabolite(s) no information

Excretion

by kidneys (5%)

Urine no information

t½ 3-4 hours

ROUTES

SC (injection)

direct IV (not currently recommended)

IM (depot injection, smallest needle = 22 gauge)

EXTRAVASATION HAZARD

none

INDICATIONS AND OTHER USES

- Prostate cancer

OTHER ONCOLOGY USES

Breast cancer

Ovarian cancer

CONTRAINDICATIONS

- known hypersensitivity to leuprolide

SIDE EFFECTS

* may be life-threatening

side effects in **bold**, *italic type* are common

IMMEDIATE ONSET (hours to days)

nausea and vomiting (depot injection)

disease flare (increased bone pain,

urinary tract obstruction, spinal cord compression)

irritation or redness (erythema) at injection site (9%)

DELAYED/LATE ONSET (weeks- years)

breast swelling or tenderness

(gynecomastia)

decrease in testicular size (atrophy, 7%)

blurred vision

EARLY ONSET (days to weeks)

swelling of hands, feet or lower legs (edema)

hot flushes (46%)***impotence and decreased sex drive (decreased libido)***

breast swelling or tenderness (gynecomastia)

decrease in testicular size (atrophy, 7%)

loss of menstruation (amenorrhea)

vaginal bleeding

constipation, loss of appetite

dizziness, depression, headache

irritability, insomnia

blurred vision

paresthesia

increased BUN and creatinine

LEUPROLIDE

CLINICAL MONITORING

RECOMMENDED CRITERIA

No Recommended Toxicity Ratings

SUGGESTED CRITERIA

No Additional Toxicity Ratings

DOSING

Subcutaneous

- daily, 1 mg (0.2 mL)
- Doses up to 20 mg/day have been used but do not improve response
- Use for about 2 weeks prior to beginning monthly treatments in those patients at risk of worsening signs and symptoms

Intramuscular

- q28-33 days, 7.5 mg (entire contents of vial of depot formulation)
- Delay of 14 days or more will result in increased testosterone levels

Pediatric: No pediatric indications

Other dosing may be indicated

SIGNIFICANT INTERACTIONS

none reported to date

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-

Community Level Take Home

Prescription (NOTE: Use of preprinted Physician Standing Order is recommended). Depot

administration in Physician's Office

CDHA Status

Formulary

Pharmacare Status

Formulary

PHARMACEUTICAL CONSIDERATIONS

Injection

5 mg/mL (2.8 mL multi-dose vial) as leuprolide acetate. protect from light (store in carton) until use; store in the refrigerator (2-8°C). Patient may store current vial unrefrigerated. Preserved with benzyl alcohol 0.9% and may contain sodium hydroxide and/or acetic acid to adjust pH.

Depot injection

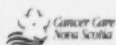
7.5 mg single-dose vial containing lyophilized microspheres of leuprolide acetate incorporated in a biodegradable copolymer of lactic acid and glycolic acids. Each mL of diluent provided contains carboxymethylcellulose sodium 5 mg, D-mannitol 50 mg, polysorbate 80 1 mg and water for injection. Store depot and diluent at room temperature.

Reconstitute depot injection with 1 mL of diluent provided (do not substitute another diluent) to a final concentration of 7.5 mg/mL. Shake well to disperse particles.

Reconstituted depot injection

Milky appearance: Due to the presence of microspheres it is necessary that a needle with an adequate gauge (ie, 22 gauge) be used. Use of a smaller needle (eg, 30 gauge) could result in clogging of the needle. Preservative-free; prepare immediately before use and discard unused portion.

It is recommended that leuprolide not be mixed with other drugs.



LIPOSOMAL DOXORUBICIN (PEGYLATED)

(Antineoplastic Agent, Anthracycline, Antibiotic)

Revision Date Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Caelyx® Vials of 20mg/10mL (Red Suspension)

MECHANISM OF ACTION

Liposomes have been shown to penetrate solid tumors more effectively, possibly because of their small size and longer circulation time. Once in tissues, doxorubicin is released. Doxorubicin inhibits DNA and RNA synthesis by intercalation between DNA base pairs and by steric obstruction; and intercalates at points of local uncoiling of the double helix. Although the exact mechanism is unclear, it appears that direct binding to DNA (intercalation) and inhibition of DNA repair (topoisomerase 2 inhibition) result in blockade of DNA and RNA synthesis and fragmentation of DNA. It is also a powerful iron chelator, the iron-doxorubicin complex can bind DNA and cell membranes and produce free radicals that immediately cleave the DNA and cell membranes.

PHARMACOKINETICS

Oral Absorption

No

Distribution

two phases: short first phase (~5 hours); prolonged second phase (~55 hours); distributed to liver, spleen, bone marrow and lungs (14.5%) as large multilamellar liposomes, PEG-coated liposomes to liver (10-15%) and RES organs (lungs (4-9%), spleen (2-8%))

tissue distribution: in AIDS-KS lesions 21 times higher than normal skin; enters breast-milk

cross blood brain barrier? No information
Vd- 2.7-2.8 L/m² PPB- no information

Metabolism

similar to doxorubicin, but metabolite plasma levels are low
major metabolite: Doxorubicinol detected in very low plasma levels inactive metabolite(s) yes

Excretion

renal

Urine: 5.5% after 72 hrs; small quantities of Doxorubicinol
 $t_{1/2\alpha}$ - 1-5.2 hrs $t_{1/2\beta}$ - 52-55 hrs
Cl- slow- 0.042 L/h/m²

IV COMPATIBILITY

dextrose 5% ONLY, do not mix with NS
do NOT use in-line filter

ROUTES

intravenous infusion over 30 minutes

ADMINISTRATION

- Mix doses <90mg in 250mL bag (5% Dextrose), or doses ≥90mg in 500mL bag (5% Dextrose).
- Infuse at initial dose at a rate no greater than 1 mg/minute over 30 minutes; if no infusion-related reaction is observed, subsequent infusions may be administered over a 60 minute period

EXTRAVASATION HAZARD

should be considered as an IRRITANT, like Doxorubicin
use same procedures as Doxorubicin- side arm free-flowing IV
Follow Extravasation Guidelines

INDICATIONS AND OTHER USES

- Ovarian cancer, advanced, failed standard first-line therapy
- AIDS-related kaposi's sarcoma, progressive disease

OTHER ONCOLOGY USES

Breast cancer

CONTRAINDICATIONS

- same as Doxorubicin

Continued Next Page...

LIPOSOMAL DOXORUBICIN (PEGYLATED)

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

- * anaphylaxis (rare)
- flare reaction (histamine release)
- pain at injection site during injection
- vein irritation (phlebitis)
- facial flushing
- nausea and vomiting**
- urine discolouration** (reddish, lasts 1-2 days)
- radiation recall reaction (rare)

EARLY ONSET (days to weeks)

- * **low WBC, RBC, platelets**
- mouth sores**
- diarrhea
- eye irritation (rare, conjunctivitis)
- alopecia

DELAYED/LATE ONSET (weeks- years)

- Hand-and-foot syndrome** (Palmar-plantar erythrodysesthesia=PPE)
- * heart problems (congestive heart failure and/or cardiomyopathy, dose-related)-rare
- darkening of skin (hyperpigmentation), nail changes
- infertility**

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Baseline liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]
- Observation for **hypersensitivity reaction, pulse rate and blood pressure** during and for 30 minutes after injection (emergency treatment readily available)

HYPERSENSITIVITY/ALLERGY

- 0 None
- 1. Transient rash, fever <38°C
- 2. Urticaria, fever ≥38°C, mild bronchospasm
- 3. Serum sickness, bronchospasm, requires parenteral medications
- 4. Anaphylaxis

Rated In Response To Patient Reaction

SUGGESTED CRITERIA

- Baseline & periodic **cardiac function tests** (Echo RNA and/or MUGA scans) for all patients with cardiac risk factors

HAND-FOOT SKIN REACTION

- 0 none
- 1 skin changes or dermatitis without pain (e.g. erythema, peeling)
- 2 skin changes with pain, not interfering with function
- 3 skin changes with pain, interfering with function

SIGNIFICANT INTERACTIONS

→no formal drug interactions have been reported with liposome-encapsulated doxorubicin specifically

Doxorubicin Interactions:
radiotherapy, digoxin, barbiturates, quinolones (norfloxacin, ciprofloxacin), cyclophosphamide, mercaptopurine, ranitidine, cimetidine

LIPOSOMAL DOXORUBICIN (PEGYLATED)

DOSING

All doses given as a single agent on Day 1

Injection (Ovarian Cancer):

- 40-50mg/m² IV q4 weeks until loss of tolerance or disease progression

AIDS-Related Kaposi's Sarcoma

- 20mg/m² IV q2-3 weeks until loss of tolerance or disease progression

Pediatric: Safety & effectiveness not established

Other dosing may be indicated

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Intermediate Level, indication
restrictions

CDHA Status Formulary- Restricted
Pharmacare Status Non-Formulary

DOSE ADJUSTMENT CRITERIA

Myelosuppression:

1. If ANC <1.0 × 10⁹/L, wait until ANC ≥1.0, then restart at a **25%** reduced dose.
2. If ANC <0.5 × 10⁹/L, wait until ANC ≥1.0, then restart at a **50%** reduced dose.

Palmar-plantar-erythrodysesthesia

1. If grade 2/3/4 after week 3 of treatment, **HOLD** dose for 1 week.

After week 4 of treatment:

2. If grade 1 **reduce** to **25%** dose; return to 3-week interval.
3. If grade 2 **reduce** to **50%** dose; return to 3-week interval.
4. If grade 3 **discontinue** the treatment.

Stomatitis:

1. If grade 2 **HOLD** dose for 1 week.
2. If grade 3 **HOLD** dose for 1 week, then **reduce** to **25%** dose.
3. If grade 4 **HOLD** dose for 1 week, then **reduce** to **50%** dose.

Hepatic dysfunction:

1. If serum bilirubin = 21 to 51 µmol/L, **reduce** to **50%** dose.
2. If serum bilirubin >51 µmol/L, **reduce** to **25%** of normal dose.

PHARMACEUTICAL CONSIDERATIONS

Injection:

2mg/mL doxorubicin HCl pegylated liposomes in vials of 20mg/10mL and 50mg/25mL. Stealth liposomes composed of N-(carbamoylmethoxypolyethylene glycol 2000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine sodium salt (MPEG-DSPE); 3.19mg/mL fully hydrogenated soy phosphatidylcholine (HSPC); 9.58mg/mL and cholesterol 3.19mg/mL. Greater than 90% of the drug is encapsulated in the Stealth liposomes. Store in refrigerator at 2-8 °C; protect from freezing. Do not shake vigorously.

Diluted solution for infusion

Dilute suspension in 5% dextrose solution (250mL D5W for <90 mg liposomal doxorubicin; 500mL D5W for ≥90 mg liposomal doxorubicin). Stable for 24 hours at room temperature or if refrigerated.

Administer IV infusion at ≤ 1mg/minute for initial infusion; if no infusion reaction, balance of dose may be given over 60 minutes. Do not use an in-line filter during intravenous infusion. Administer through side arm of 5% Dextrose infusion.

Do not mix with any other drugs, bacteriostatic agents (benzyl alcohol) or any other solution.

LOMUSTINE

(Antineoplastic Agent, Alkylating Agent (Nitrosourea))

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: CeeNU® White capsules with 10mg, white/green capsules with 40mg, pale green capsules with 100mg Lomustine

Also known as CCNU

MECHANISM OF ACTION

A nitrosourea agent, lomustine acts by both alkylation and carbamylation. It appears to alkylate DNA, prevent DNA repair, and alter the structure of RNA and the structure and function of a variety of enzymes and proteins. It appears that carbamylation of DNA polymerase, not DNA structure modifications, are responsible for the inhibition of DNA synthesis. It is cell-cycle nonspecific, but may be active primarily in late G1 or early S phase.

PHARMACOKINETICS

Oral Absorption

rapidly and completely absorbed (in 30-60 minutes)

Distribution

highly lipid soluble, rapid and extensive tissue distribution; enters breast-milk, cross blood brain barrier?

CSF achieves 50% of plasma levels

Vd- no information PPB- 50%

Metabolism

actively metabolized by hepatic microsomal enzyme oxidation system and GI; significant first pass effect
metabolite(s): active- cis-4-hydroxy-CCNU and trans-4-hydroxy CCNU
inactive- yes

Excretion

renal 50%, respiratory <10%, biliary <5%
Urine 50% within 24 hours, as metabolites

t_{1/2} α Lomustine: 16-72 hours,

metabolites: 1-3-2 days

elimination t_{1/2}: 1-3-2 9 hours

t_{1/2} β lomustine: 0.25 hour,

metabolites: 16-50 hours

SIGNIFICANT INTERACTIONS

cimetidine, phenobarbital, melphalan, radiation sensitizers, theophylline
Cytochrome P450 2D6 Inhibitor

DOSE ADJUSTMENT CRITERIA

Renal failure (Suggested action)

If CrCl <12mL/min or Serum Creatinine >150μmol/L, reduce Lomustine to **25-50%** dose, or reconsider use of Lomustine

ROUTES

oral

INDICATIONS AND OTHER USES

- Brain tumours
- Breast cancer
- Hodgkin's disease
- Lung cancer
- Malignant melanoma
- Multiple myeloma
- Non-Hodgkin's lymphomas
- Ovarian cancer
- Pancreatic cancer
- Renal cell cancer

CONTRAINDICATIONS

- known hypersensitivity to lomustine or other nitrosoureas
- pregnancy and breast feeding
- low WBC, RBC, platelets (myelosuppression)

DOSING

As a single dose, nausea may be minimized by giving at bedtime on an empty stomach. If the patient vomits after 30-45 minutes, do not repeat the dose. Dose should be calculated to the nearest 10 mg to accommodate capsule sizes.

Other dosing may be indicated

Oral:

- q6w: 130 mg/m² po

Pediatric:

Dose should be calculated to the nearest 10 mg to accommodate capsule sizes.

- q6w: 100 mg/m² po

Continued Next Page...

LOMUSTINE

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)
nausea and vomiting (54%, onset 45 minutes to 6 hours, may last 24 hours)

EARLY ONSET (days to weeks)
mouth sores (rare, stomatitis)
liver problems (transient elevation of liver function tests)

DELAYED/LATE ONSET (weeks- years)
* **low WBC, RBC, platelets**
(**myelosuppression**, nadir 24-60 days, recovery 38-65 days)
lung problems (rare, infiltrates and/or fibrosis)
kidney problems
liver problems (transient elevation of liver function tests)
mouth sores (rare, stomatitis)
hair loss (rare, alopecia)
CNS problems (rare)
infertility
* cancer (leukemia)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Periodic clinical pulmonary exam, including auscultation, pulmonary toxicity ratings (Cough, SOB)- if treatment for >6mo
- Baseline renal function tests (if failure suspected) [serum creatinine, electrolytes & BUN]

COUGH

- 0 None
- 1 Mild
- 2 Moderate
- 3 Severe

SHORT OF BREATH

- 0 No change
- 1 Mild SOB
- 2 Dyspnea on exertion
- 3 Dyspnea at normal level of activity
- 4 Dyspnea at rest

At Each Clinic Visit After 6 Months' Treatment

SUGGESTED CRITERIA

- Periodic renal function tests [serum creatinine, electrolytes & BUN]
- Periodic liver function tests [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]

ANTIEMETIC RISK

HIGH RISK (30-90% of patients)

- Use a serotonin receptor antagonist PLUS dexamethasone pre-chemotherapy and post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

PHARMACEUTICAL CONSIDERATIONS

Capsules

10 mg, 40 mg and 100 mg; store at room temperature, protected from light and from excessive heat (over 40°C); contain mannitol and magnesium stearate

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status- Community Level. Take home prescription on preprinted Physician Standing Order

CDHA Status Formulary
Pharmacare Status Formulary

NOTE: It is recommended to limit ordering of this medication to preprinted Physician Standing Order form, for patient safety

LOPERAMIDE

(Antidiarrheal)

Revision Date, Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Imodium®

Green caplets of 2mg Loperamide

Generic products available

MECHANISM OF ACTION

Loperamide slows intestinal motility and affects water and electrolyte movement through the bowel. It inhibits peristalsis by a direct effect on the circular and longitudinal muscles of the intestinal wall. It reduces daily fecal volume, increases viscosity and bulk density and diminishes the loss of fluid and electrolytes.

PHARMACOKINETICS

Oral Absorption

oral 40%

Distribution

No information.

Excretion in breast-milk or if it crosses the placenta is unknown
cross blood brain barrier? Does not penetrate well into the brain

Metabolism

No information

Excretion

less than 2% is excreted in urine and 30% in feces as intact drug

Urine: less than 2%

t½ 10.8 hours (9.1-14.4)

ROUTES

oral

INDICATIONS AND OTHER USES

- Symptomatic control of diarrhea

OTHER ONCOLOGY USES

Management of chemotherapy-induced diarrhea

CONTRAINDICATIONS

- acute ulcerative colitis
- abdominal distension
- constipation
- ileus
- pseudomembranous colitis associated with broad-spectrum antibiotics
- patients for whom constipation must be avoided
- acute diarrhea associated with organism that penetrate the intestinal mucosa (enteroinvasive *Escherichia coli*, salmonella and *Shigella*)
- children under 2 years old

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

Minor:

abdominal pain, distention or discomfort, constipation, drowsiness, dizziness, fatigue, dry mouth, nausea, vomiting, epigastric pain

CLINICAL MONITORING

RECOMMENDED CRITERIA

NO RECOMMENDED TOXICITY RATINGS

SUGGESTED CRITERIA

- For patients with hepatic dysfunction: monitor for signs and symptoms of CNS toxicity or CNS depression (first 24 hours of treatment)

LOPERAMIDE

DOSING

Oral:

- 4mg initial dose, followed by 2mg after each loose stool. Maximum of 16mg (8 tablets) daily for symptomatic relief of diarrhea.
- 4mg initial dose upon loose stools or change in bowel habit, followed by 2mg q2h (or 4mg q4h overnight) until 12 hours after bowel return to normal habits- with irinotecan-based chemotherapy (or other chemotherapy for colon cancer)

Other dosing may be indicated

PHARMACEUTICAL CONSIDERATIONS

Tablets: 2mg green capsule-shaped tablets; bisulfites-, gluten-, lactose-, sodium-, and tartrazine-free. Store at room temperature; protect from light.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level: Take Home
Prescription, Over the Counter
CDHA Status Formulary
Pharmacare Status Formulary

MECHLORETHAMINE

(Antineoplastic Agent; Alkylating Agent (Nitrogen Mustard))

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Mustargen® Vials with 10mg Mechlorethamine for reconstitution with sterile water for injection

MECHANISM OF ACTION

Mechlorethamine is a bifunctional alkylating agent that inhibits DNA and RNA synthesis via formation of carbonium ions; produces inter- and intrastrand cross-links in DNA resulting in miscoding, breakage, and failure of replication. Although not cell cycle specific per se, its effect is most pronounced in the S phase, and cell proliferation is arrested at the G2 phase.

PHARMACOKINETICS

Oral Absorption

yes but extremely irritating to tissues

Distribution

not elucidated, highly reactive drug which is cleared from the blood within minutes

Excretion in breast-milk unknown

cross blood brain barrier? no information

Vd, PPB- no information

Metabolism

rapid hydrolysis and demethylation,

possibly in the plasma

ionizes in solution to active form and

combines with reactive compounds

metabolite(s): active, inactive- yes

Excretion

<0.01% of dose is excreted unchanged by the kidneys; about 0.01% of dose is excreted in the bile

Urine: 50% (as metabolites) within 24 hours $t_{1/2}$ <1 min

SIGNIFICANT INTERACTIONS

muscle relaxants, thiols

EXTRAVASATION HAZARD

VESICANT (tissue damage on extravasation)

Management- stop IV, aspirate, elevate limb, cold intermittent compresses

Follow Extravasation Guidelines

ANTIEMETIC RISK

HIGH RISK (30-90% of patients)

- Use a serotonin receptor antagonist PLUS dexamethasone pre-chemotherapy and post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

IV COMPATIBILITY

normal saline

ROUTES

topical (10 mg in 45-60 mL tap water)

direct IV (push slowly, check for blood return every 2-3 mL)

intermittent IV (preferred route, in 100 mL over 30 minutes)

intraperitoneal

(in 50-100 mL NS, positional changes q5-10 min x 1 hour, dwell time 24-36 hours)

intrapleural

(in 100 mL NS, positional changes q5-10 min x 1 hour)

ADMINISTRATION

- Slow push through sidearm of free flowing IV (5% Dextrose, Normal Saline); Infuse slowly; Administer within 15 minutes of reconstitution (*administering nurse should be certified to administer IV push chemotherapy agents*)
- Slow down injection/infusion rate if erythematous streaking occurs

DOSING

Intravenous:

- q3-6w: 0.4 mg/kg
- q4w: 6 mg/m² on day 1 or on days 1 and 8

Pediatric

Intravenous:

- q4w: 6 mg/m² weekly
- Other dosing may be indicated

MECHLORETHAMINE

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

* anaphylaxis (rare)

vein irritation (phlebitis, pain)

flare reaction (erythema, pruritus,

urticaria, venous streaking)

nausea and vomiting (>90%,

onset 1-3 hours, duration 8-24 hours,

may be severe)

metallic taste

central nervous system problems

(drowsiness, tinnitus, hearing loss)

EARLY ONSET (days to weeks)

* **low WBC, RBC, platelets**

(**myelosuppression**, nadir 7-14 days,

recovery 28 days)

vein irritation (sclerosis)

mouth sores (rare, stomatitis)

loss of appetite (anorexia) diarrhea

skin problems (rash, contact dermatitis

with topical use)

increased uric acid levels

(hyperuricemia)

hair loss (rare, alopecia)

DELAYED/LATE ONSET (weeks to years)

infertility

skin problems (contact dermatitis with topical use)

cancer (leukemia, lymphoma, skin cancer)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment

SUGGESTED CRITERIA

- Baseline & periodic Hearing ratings.
- **hearing tests** if symptomatic
- Local Site Toxicity ratings, if incident of phlebitis

HEARING

- 0 No change
- 1 Asymptomatic
- 2 Tinnitus
- 3 Correctable hearing loss
- 4 Deafness

Rated At Clinic Visits Every 2-3 Months

LOCAL SITE TOXICITY

- 0 None
- 1 Pain
- 2 Pain & inflammation, phlebitis
- 3 Ulceration
- 4 Plastic surgery

Upon Patient Complaint Or Clinical Event

INDICATIONS AND OTHER USES

- Hodgkin's disease
- Mycosis fungoides
- Chronic lymphocytic leukemia
- Chronic myelogenous leukemia
- Lung cancer, small cell
- Malignant effusions
- Medulloblastoma
- Non-Hodgkin's lymphoma
- Polycythemia rubra vera

CONTRAINDICATIONS

known hypersensitivity to
mechlorethamine
pregnancy and breast feeding
low WBC, RBC, platelets
(myelosuppression)
muscle relaxants, thiols

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Intermediate Level

CDHA Status Formulary

Pharmacare Status Formulary (red)

DOSE ADJUSTMENT CRITERIA

Renal or hepatic dysfunction

No adjustment required

(Suggested action)

Continued Next Page...

MECHLORETHAMINE**PHARMACEUTICAL CONSIDERATIONS****Injection**

10 mg; store at room temperature.

Reconstitute powder with 10 mL NS or SWI to a final concentration of 1 mg/mL. No other solutions should be used to reconstitute since rapid decomposition will occur. Do not use if solution is discoloured.

Reconstituted solution for injection

Reconstitute immediately before use (within 5 minutes) and discard unused portion of vial. Losses of 8-10% at 22°C and 4-6% at 4°C have been reported when mechlorethamine 1 mg/mL was stored in vials or plastic syringes for 6 hours.

Diluted solution for infusion

May be diluted in 50 or 100 mL NS. Stable in NS at a concentration of 0.1 mg/mL for one hour at room temperature (7% loss of mechlorethamine).

Compatible with ondansetron. It is recommended that mechlorethamine not be mixed with other drugs.



MEDROXYPROGESTERONE

(Contraceptive, Oral Progestin)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Provera® White tablets with 100mg, also orange tablets with
Generic products available 2.5mg, blue tablets with 5mg, white tablets with 10mg

MECHANISM OF ACTION

Inhibits secretion of pituitary gonadotropins, which prevents follicular maturation and ovulation, stimulates growth of mammary tissue.

PHARMACOKINETICS

Oral Absorption

rapid, subject to first-pass metabolism in the liver

Distribution

not elucidated, detectable in breast milk
cross blood brain barrier? no information
Vd, PPB- no information

Metabolism

promptly metabolized in liver, first pass effect

metabolite(s) active- no; inactive- yes

Excretion

urine (20-40%) and feces (5-13%)

Urine: 20-42%

t_{1/2} apparent t_{1/2} 30 hours

ROUTES

oral (divided doses)
intramuscular (deep IM, rotate gluteal sites)

DOSING

daily 2.5 mg (replacement therapy)

Oral:

- daily: usual 200-400 mg (range 200-2400 mg) in divided doses three times weekly (tiw): 500 mg

Intramuscular:

- daily: 500 mg/day x 28 days then 500 mg twice weekly (biw)
- q1-4w: 400-1000 mg

Adequate trial 8-12 weeks

Pediatric: No pediatric indications

Other dosing may be indicated

INDICATIONS AND OTHER USES

- Breast cancer
- Endometrial cancer
- Renal cell cancer

CONTRAINDICATIONS

- pregnancy and breast feeding
- history of thromboembolic disorders, thrombophlebitis or cerebral apoplexy (stroke)
- undiagnosed vaginal bleeding
- undiagnosed urinary tract bleeding

SIGNIFICANT INTERACTIONS

severe liver (hepatic) failure
aminoglutethimide, antidepressants,
rifampin, thyroid function test, tamoxifen,
warfarin, other antineoplastic agents
Cytochrome P450 1A Inducer

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Baseline pregnancy test

MEDROXYPROGESTERONE

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET

nausea and vomiting (54%, onset 45 minutes to 6 hours, may last 24 hours)

EARLY ONSET

(days to weeks)

- * anaphylaxis (rare)
- nausea (rare)
- pain at injection site

DELAYED/LATE ONSET (weeks- years)

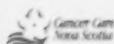
fluid retention (edema, weight gain)

- * blood clots (thrombophlebitis, pulmonary embolism)
- sterile abscess at injection site
- breast tenderness, discharge from the nipple (rare, galactorrhea)
- breakthrough bleeding, loss of menses (amenorrhea)
- central nervous system problems (depression, headache, dizziness, fatigue, insomnia, nervousness)
- appetite changes (weight gain), loss of diabetic control
- liver problems (elevated liver function tests)
- increased serum calcium levels (hypercalcemia)
- skin problems (rare, acne), hair loss (rare, reversible alopecia)

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level Take Home
Prescription (NOTE: Use of
preprinted Physician Standing Order
for oncology indications is
recommended)

CDHA Status	Formulary
Pharmacare Status	Formulary



MEGESTROL

(Antineoplastic Agent, Hormone, Appetite Stimulant, Progestin) Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Megace® Blue round tablets with 40mg, white oval tablets with 160mg
Generic products available

MECHANISM OF ACTION

The exact mechanism as an antineoplastic agent is unknown. The drug is a synthetic progestogen; pituitary inhibition as a consequence of an antiluteinizing effect has been postulated.

PHARMACOKINETICS

Oral Absorption

rapid and extensive

Distribution

found in breast milk

cross blood brain barrier? no information

Vd, PPB- no information

Metabolism

mainly in liver to free steroids and
glucuronide conjugates

metabolite(s): active- no inactive- yes

Excretion

renal (57% to 78%), hepatic (8% to 30%)

Urine: 66.4% within 10 days

t½ 15-100hours

ROUTES

oral

DOSING

Oral

• daily: 120-160 mg (range 40-320 mg)

• bid: 80 mg (range 40-160 mg)

• qid: 40 mg

Adequate trial: 2 month

Cachexia

• daily: 480-800 mg po (nb, this use is
still under active investigation)

Pediatric: No pediatric indications

Other dosing may be indicated

SIDE EFFECTS

* may be life-threatening

side effects in ***bold, italic*** type are common

IMMEDIATE ONSET (hours to days)

mild nausea (7%)

DELAYED/LATE ONSET (weeks- years)

* blood clots (deep vein thrombosis, rare)

hair loss (alopecia)

vaginal bleeding (upon withdrawal)

EARLY ONSET (days to weeks)

fluid retention (10-20%, edema)

carpel tunnel syndrome (rare)

hot flushes (rare)

increased serum calcium levels (with
bone metastases, hypercalcemia)

improved appetite and weight gain
(15-70%)

Sensitivity to sunlight

SIGNIFICANT INTERACTIONS

aminoglutethimide, vincristine

INDICATIONS AND OTHER USES

- Breast cancer
- Endometrial cancer
- Prostate cancer

OTHER ONCOLOGY USES

Cancer cachexia

CLINICAL MONITORING

NO RECOMMENDED TOXICITY
RATINGS

CONTRAINDICATIONS

- known hypersensitivity to megestrol
- pregnancy and breast feeding
- history of significant thromboembolic disease

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-

Community Level: Take Home

Prescription (NOTE: Use of
preprinted Physician Standing Order
for oncology indications is
recommended)

CDHA Status Formulary

Pharmacare Status Formulary

MELPHALAN

(Antineoplastic Agent: Alkylating Agent (Nitrogen Mustard)) Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Alkeran® White tablets with 2mg. Vials with 50mg for reconstitution with 10mL solvent diluent provided

MECHANISM OF ACTION

Alkylating Agent which is a derivative of mechlorethamine that inhibits DNA and RNA synthesis via formation of carbonium ions, cross-links strands of DNA

PHARMACOKINETICS

Oral Absorption

incomplete, variable, 25-89% post oral dose; AUC decreased by 39% when taken with food

Distribution

rapid distribution into total body water; excretion in breast-milk unknown; cross blood brain barrier? no information; Vd- 0.5-0.6 L/kg, 14.6±5.1 L/m²; PPB- 90±5%

Metabolism

not actively metabolised; spontaneously degrades to mono and dihydroxy products; primary means of elimination; metabolite(s) active, inactive- no

Excretion

mainly feces (20-50% within 6 days) and urine

feces: 20-50% within 6 days
t_{1/2} 8 minutes (IV) t_{1/2} β 1.8 hours (IV)

Urine: 10-30% as intact drug in 24 hours
Cl- 5.2±2.9 mL/min/kg;
0.438±0.178 L/min/m²

IV COMPATIBILITY

normal saline only

ROUTES

oral (on an empty stomach)
direct IV (over 5 minutes)
intermittent IV (in 100 mL over 15 minutes)
intraperitoneal (refer to monograph)

ADMINISTRATION

- Slow push through sidearm of free flowing IV (Normal Saline) over 1-4 minutes (*administering nurse should be certified to administer IV push chemotherapy agents*)
- Reconstitute powder with 10mL of diluent solution, then immediately dilute dose in Normal Saline to a concentration >0.45mg/mL. Infuse within 1 hour of reconstitution
- Mix in 50-100mL bag (Normal Saline); infuse over 15-30 minutes
- Protect from light

EXTRAVASATION HAZARD

VESICANT (tissue damage on extravasation)

Management- stop IV, aspirate, elevate limb, cold intermittent compresses
Follow Extravasation Guidelines

SIGNIFICANT INTERACTIONS

cimetidine, cyclosporine, food, interferon alfa, nalidixic acid, prednisolone, other antineoplastic agents
(with high dose melphalan, avoid other quinolones such as ciprofloxacin, norfloxacin and ofloxacin)

ANTIEMETIC RISK

- Oral Doses- LOW RISK (Less than 10% of patients)
- No routine antiemetic pre-chemotherapy or post-chemotherapy
- IV Doses- HIGH RISK (30-90% of patients)
- Use a serotonin receptor antagonist PLUS dexamethasone pre-chemotherapy and post-chemotherapy
- See Nausea & Vomiting Guidelines for more detail



MELPHALAN

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)

- * anaphylaxis (rare)
- nausea and vomiting (rare with chronic low doses)

DELAYED/LATE ONSET (weeks- years)

- loss of menstruation (amenorrhea)
- infertility
- * lung problems (chronic fibrosis, rare)
- * acute leukemia

EARLY ONSET (days to weeks)

- * **low WBC, RBC, platelets** (**myelosuppression** nadir 10-21 days, recovery 18-40 days)
- mouth sores (stomatitis)**
- diarrhea
- darkening of skin (hyperpigmentation)**
- skin rash
- hair loss (alopecia, BMT doses)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC), serum electrolytes and serum uric acid levels** before each cycle of treatment

SUGGESTED CRITERIA

- Baseline **renal function tests**- intravenous doses only [serum creatinine, electrolytes & BUN]

DOSING

Intravenous injection

- Single IV administration of 1 mg/kg.
- Refractory Multiple Myeloma: 50 - 100 mg/m²

Oral:

- q4w: 9 mg/m²/day po x 4 days, escalate to 12 mg/m²/day
- q4-5w: 2 mg/kg/day po x 5 days
- daily: 4 mg/m² po
- single daily dose, on empty stomach preferable

Adequate trial:

- response may be gradual over many months

Intra-arterial perfusion:

- q3w: 70-100 mg x 2-3 cycles

Bone marrow transplant:

- much higher doses are used for tumour ablation prior to marrow transplant than for standard treatment regimens, eg, 100 mg/m² IV (range 40-200 mg/m² IV) may be used alone or in combination with other cytotoxic drugs.

Pediatric

Oral:

- daily: 4-20 mg/m² x 1-21 days

Intravenous:

- q3-4w: 30-45 mg/m²

Bone marrow transplant:

- 40-70 mg/m²/day IV x 3 days or 110-180 mg/m² IV x 1 day

Other dosing may be indicated

DOSE ADJUSTMENT CRITERIA

Renal failure: (Suggested action)

1. If CrCl = 0.2-0.8 mL/sec. **REDUCE to 75% dose**
2. If CrCl < 0.2 mL/sec. **REDUCE to 50% dose (intravenous doses only)**

CONTRAINDICATIONS

- known hypersensitivity to melphalan
- pregnancy and breast feeding
- low WBC, RBC, platelets (myelosuppression)

Continued Next Page...

MELPHALAN

PHARMACEUTICAL CONSIDERATIONS

Tablets. 2 mg; store at room temperature (15-25°C); protect from light and moisture. The manufacturer recommends that melphalan be dispensed in glass. Tablets contain lactose, sucrose, potato starch, povidone, and magnesium stearate.

Injection

Package of one vial containing melphalan 50 mg with 20 mg povidone K12 and one vial containing 10 mL of buffer solution (60% w/v propylene glycol with sodium citrate and ethanol); store at room temperature; protect from light. Refrigeration of the package may result in incomplete dissolution of the melphalan.

Reconstitute powder with 10 mL of the diluent provided to a final concentration of 5 mg/mL. Do not use any other diluent.

Reconstituted solution for injection

Reconstituted solution should be used as soon as possible. Trissel reports a 10% potency loss approximately 3 hours after reconstitution. Storage of the reconstituted solution in the refrigerator will result in precipitation. Solutions that appear turbid or contain crystals should be discarded.

Diluted solution for infusion

The manufacturer states that further dilution of the reconstituted solution results in decreased stability and that, if necessary to dilute further, only NS should be used. Administration should be completed within 1.5 hours of reconstitution. Trissel recommends a maximum concentration of 2 mg/mL in NS and states that dilution in NS, D5W, or lactated Ringer's at 25°C resulted in 10% decomposition in 2.4, 0.6 and 1.5 hours, respectively. Storage at temperatures greater than 25°C will increase the rate of degradation of melphalan. Freezing a 20 mcg/mL solution of melphalan in NS and storing at -20°C for 6 months resulted in insignificant decomposition (2-4% loss). Trissel recommends filtration of the reconstituted solution through a 0.45 micron solution during the dilution step and reports that filtration of a 20 mcg/mL solution in NS through a 0.2 micron cellulose acetate filter delivered 99% of the initial concentration.

Melphalan injection has reduced stability and the rate of degradation increases rapidly with rise in temperature.

It is recommended that melphalan not be mixed with other drugs.

INDICATIONS AND OTHER USES

- Multiple myeloma
- Ovarian cancer

OTHER ONCOLOGY USES (Not Approved)

Acute lymphoblastic leukemia (ALL)

Breast cancer

Ewing's sarcoma

Hodgkin's disease

Malignant melanoma

Neuroblastoma

Non-Hodgkin's lymphomas

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-

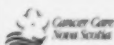
Injection- Advanced Level;

Oral- Community Level; Take home prescription on preprinted Physician Standing Order

CDHA Status Formulary

Pharmacare Status Formulary

NOTE: It is recommended to limit ordering of this medication to pre-printed Physician Standing Order form, for patient safety



MERCAPTOPURINE

(Antineoplastic Agent; Antimetabolite)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Purinethol® Pale yellow tablets with 50mg Mercaptopurine

MECHANISM OF ACTION

Mercaptopurine is a purine antagonist that inhibits DNA and RNA synthesis; acts as a false metabolite for hypoxanthine and is incorporated into DNA and RNA, eventually inhibiting synthesis; specific for the S phase of the cell cycle.

PHARMACOKINETICS

Oral Absorption

incomplete and variable (16% to 50%)
 bioavailability 5-37% largely due to first pass metabolism in the liver (less when given with food)

Distribution

widely distributed to body tissues, found in breast milk

cross blood brain barrier?

negligible with conventional doses.
 cytotoxic concentrations reached with high IV doses

Vd- 0.56-0.9 L/kg total body water

PPB- 19-30%

Metabolism

in the GI tract and liver via xanthine oxidase and methylation to sulfate conjugates, 6-thiouric acid, and other inactive compounds

metabolite(s): active- 6-thioinosinic acid, 6-thioguanilic acid

inactive- 6-thiouric acid, 6-methylthiopurine derivatives

Excretion

At conventional doses clearance is primarily hepatic. Renal clearance may become important at high doses.

Renal: following high (1 g/m²) I.V. doses, 20% to 40% of dose is excreted unchanged in the urine; at lower doses, renal excretion is minor.

Urine: 50% of oral dose in 24 hours,

20%-40% of dose (high I.V. dose)

t_{1/2} age-dependent:

children: 21 min, adults: 47 min

Cl- 11±4 mL/min/kg

IV COMPATIBILITY

normal saline, dextrose 5%, dextrose/saline

ROUTES

oral (on an empty stomach)
 intermittent IV (≤2 mg/mL by slow IV infusion)

EXTRAVASATION HAZARD

none

INDICATIONS AND OTHER USES

- Acute lymphocytic leukemia
- Acute myelogenous leukemia
- Chronic myelogenous leukemia

OTHER ONCOLOGY USES

Histiocytosis X

CONTRAINDICATIONS

- severe liver disease
- known hypersensitivity to mercaptopurine
- pregnancy and breast feeding

SIGNIFICANT INTERACTIONS

allopurinol (reduce dose of mercaptopurine to 25% of usual dose)
 anticoagulants (warfarin), cotrimoxazole, doxorubicin, hepatotoxic drugs, food, nucleoside analogs (e.g. vidarabine)

ANTIEMETIC RISK

LOW RISK (Less than 10% of patients)

- No routine antiemetic pre-chemotherapy or post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

DOSE ADJUSTMENT CRITERIA

Renal failure: (Suggested action)

Consider dose reduction if renal function is reduced (eg. reduced creatinine clearance/serum creatinine)

Continued Next Page...

MERCAPTOPURINE

SIDE EFFECTS

- * may be life-threatening

side effects in ***bold, italic*** type are common

IMMEDIATE ONSET (hours to days)

nausea and vomiting (mild, rare in children)

increased uric acid levels

(***hyperuricemia***)

vein irritation (IV route)

drug fever (rare)

radiation recall reaction (rare)

DELAYED/LATE ONSET

- * liver problems (cholestatic jaundice, hepatic necrosis)

EARLY ONSET (days to weeks)

- * ***low WBC, platelets***

(***myelosuppression***, nadir 7-14 days, recovery 14-21 days)

- * liver problems (cholestatic jaundice, hepatic necrosis, elevated liver function tests)

skin problems (hyperpigmentation, rash)

hair loss (alopecia) diarrhea

mouth sores (stomatitis, rare)

loss of appetite (anorexia)

inflammation of pancreas (pancreatitis)

blood in urine (hematuria, with high dose IV)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC) and serum uric acid levels** before each cycle of treatment

SUGGESTED CRITERIA

- Baseline and periodic **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]
- Baseline **renal function tests** (if failure suspected) [serum creatinine, electrolytes & BUN]
- Baseline and periodic **urinalysis tests**

DOSING

- daily as a single dose on an empty stomach
 - round to the nearest 25 mg = ½ tab
- Induction:**
- daily: 2.5 mg/kg/day po x 4 weeks, then titrate to toxicity/response (5 mg/kg/day)
 - daily: 50-100 mg/m² **Other dosing may be indicated**

Maintenance:

- daily: 1.5-2.5 mg/kg

Pediatric

Oral:

- daily: 2.5-5 mg/kg or 70 mg/m², preferably at bedtime
- decrease dose by 50% in children less than 3 months of age

Intravenous:

- q2-5w: 200 mg/m² IV over 20 minutes, then 800 mg/m² over 8 hours

PHARMACEUTICAL CONSIDERATIONS

Tablets: 50 mg, store at room temperature (15-25°C) and keep dry. Tablets contain lactose, potato starch, corn starch, stearic acid and magnesium stearate.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level. Take home
prescription on preprinted Physician
Standing Order

CDHA Status Formulary
Pharmacare Status Formulary

NOTE: It is recommended to limit ordering of this medication to pre-printed Physician Standing Order form, for patient safety

MESNA

(Antidote- Phosphoramidate Mustard-induced Hemorrhagic
Cystitis, Antineoplastic Protective Agent)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Uromitexan® Ampuls with 400mg/4mL, 1000mg/10mL Mesna

MECHANISM OF ACTION

In blood, Mesna is oxidized to dimesna which is chemically less reactive than mesna; dimesna is reduced in the kidney back to mesna, supplying a free thiol group which binds to and inactivates acrolein, the urotoxic metabolite of ifosfamide and cyclophosphamide.

PHARMACOKINETICS

Oral Absorption

50% bioavailability (ie, oral dose usually 2 x IV dose); provides lower but more prolonged urinary levels with total urinary recovery comparable to IV

Distribution

hydrophilic, does not enter most cells (ie, remains in intravascular space); dimesna enters renal tubular cells; Excretion in breast-milk unknown cross blood brain barrier? no Vd- 0.65 L/kg

PPB- Mesna/Dimesna 10%

Metabolism

rapidly oxidized in plasma to dimesna, then partially reduced back to mesna in the kidneys

metabolite(s): active- no
inactive- dimesna, only metabolite

Excretion

rapidly cleared from plasma, filtered by glomerulus and partially (33%) reduced back to mesna in renal tubules, then secreted into urine

Urine: IV: 35% mesna and 33% dimesna within 24 hours;

Oral: 42% to 53% mesna and 21% dimesna

t½ - Mesna: 22 min, Dimesna: 1.2 hours

Cl- 0.41 L/kg/h; the minimum oroprotective mesna concentration is reported to be 1.7 umol/mL or 100 mcg/mL; these conc. Are achieved with a variety of dosing regimens

SIGNIFICANT INTERACTIONS

test for ketones in urine
cisplatin

IV COMPATIBILITY

normal saline, dextrose 5%, lactated Ringer's, ifosfamide, cyclophosphamide

ROUTES

oral (dilute injection in juice, cola or milk)
direct IV (over 3-5 minutes)
intermittent IV (over 15 minutes or less)
continuous IV (over 1-36 hours)

ADMINISTRATION

- May be diluted in 50-100mL bag (5% Dextrose, Normal Saline); Infuse over 15 minutes
- May be diluted in larger volumes for continuous infusion over 6-24 hours; May be infused using an ambulatory infusion pump over longer periods (concentration should be ≥ 1 mg/mL)
- May be given as IV push through side arm of free-flowing IV over 3-5 minutes (physician only)
- May be infused concurrently with ifosfamide

EXTRAVASATION HAZARD

none when diluted
IRRITANT when undiluted
Management- stop IV, aspirate, elevate limb, cold intermittent compresses
Follow Extravasation Guidelines

INDICATIONS AND OTHER USES

- Prevention of hemorrhagic cystitis secondary to cyclophosphamide or ifosfamide

CONTRAINDICATIONS

- known hypersensitivity to mesna or other thiol compounds

Continued Next Page...

MESNA

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET

(hours to days)

nausea and vomiting
diarrhea
injection site problems (irritation, when
given undiluted)

EARLY ONSET

(days to weeks)

allergic reactions (urticaria, macular
erythematous rash)

CLINICAL MONITORING

RECOMMENDED CRITERIA

NO RECOMMENDED TOXICITY
RATINGS

SUGGESTED CRITERIA

NO ADDITIONAL TOXICITY RATINGS

(Cystitis toxicity rated for associated antineoplastics)

DOSING

Intravenous bolus:

- 20% (eg, 10-12 mg/kg) IV at 0, 4 and 8 hours
- 40% at 0, 1, 4 and 7 hours

Continuous IV:

- 20% IV immediately pre-chemo, then 50-100% with chemo, then
- 25-50% for 12 hours following chemo

Oral:

- 20% IV at hour 0, 4 and 8 hours
- Mix parenteral product with juice, cola or milk to mask its unpleasant taste. Vomiting within 1 hour of oral mesna should be reported to the physician so that IV mesna can be given.

- *Bone marrow transplant:*

- much higher doses are used prior to marrow transplant than for standard treatment regimens; eg, higher and/or more frequent doses

Pediatric

- Given at 60-160% of oxazophosphorine dose.
25% of the total dose is given concurrent with ifosfamide or cyclophosphamide and the remainder can be divided into 3 bolus doses q3-4h; or the remainder can be given as a continuous infusion over 8-12 hours. Bolus dosing and oral dosing may facilitate out-patient management

Other dosing may be indicated in specific regimens

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Basic Level (supportive care for
some chemotherapy agents)

CDHA Status

Formulary

Pharmacare Status

Non-Formulary

MESNA**PHARMACEUTICAL CONSIDERATIONS****Injection**

100 mg/mL preservative-free solution in 4 mL and 10 mL ampuls. Also contains disodium edetate and sodium hydroxide. Store at room temperature.

Oral

Injection solution, diluted in juice, cola or milk, may be taken orally. Such dilutions are reported to be stable for at least 24 hours but the solution containers should be capped to prevent oxidation of the mesna.

Storage in syringes

Extended storage of mesna (for over 12 hours at room temperature) in a plastic syringe with tip cap may result in the formation of dark or thread-like particles and a viscosity change. Similar behaviour may also occur in glass syringes. However, stability of at least 10 days in an air-free polypropylene syringe under refrigeration, room or body temperature has been reported. Concentrations of 0.6 and 20 mg/mL in D5W, NS, SWI or lactated Ringer's are chemically stable in polypropylene syringes for at least 24 hours at 30°C. The combination of ifosfamide 50 mg/mL and mesna 40 mg/mL is reported to be stable in a syringe for 7 days at room temperature or refrigerated.

Diluted solution for infusion:

Compatible for at least 24 hours at room temperature with D5W, NS, 5% dextrose in 0.45% sodium chloride and lactated Ringer's. Light protection is not required. The manufacturer recommends that dilutions of mesna should be 1 mg/mL or greater and should be used within 24 hours of preparation.

Compatible with ifosfamide or cyclophosphamide for at least 24 hours at room temperature in PVC containers. It is recommended that mesna not be mixed with other drugs. Incompatible with cisplatin.

METHOTREXATE

(Antineoplastic Agent, Antimetabolite)

Revision Date: Feb 03

DRUG

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Methotrexate Yellow tablets with 2.5mg Methotrexate
Generic products available Multidose vials with 50mg/2mL, 500mg/20mL,
1000mg/40mL, 5000mg/200mL

Also known as Amethopterin

For intrathecal use: Vials of 20mg for reconstitution, Vials of 20mg/2mL unpreserved solution

MECHANISM OF ACTION

Methotrexate is a folate antimetabolite that inhibits DNA synthesis. Methotrexate irreversibly binds to dihydrofolate reductase, inhibiting the formation of reduced folates, and thymidylate synthase, resulting in inhibition of purine and thymidylc acid synthesis. It is cell cycle specific for the S phase of the cycle.

PHARMACOKINETICS

Oral Absorption

well absorbed <30 mg/m², 20% >80 mg/m², bioavailability decreased by food and milk

Distribution

highest levels kidney, gallbladder, spleen, liver and skin, retained in liver for prolonged periods, crosses placenta, found in breast milk and malignant effusions

cross blood brain barrier? poorly

Vd- 0.4-0.8 L/kg, 16.4 L/m² PPB- 50%

Metabolism

<10% of dose is metabolized, converted to 4-deoxy-4-amino-N10-methyl pteronic acid (DAMPA) by carboxypeptidase (GI-tract), to 7-hydroxymethotrexate by aldehyde oxidase (liver) and polyglutamated intracellularly
metabolite(s): active, inactive- yes

Excretion

excreted principally by the kidney (80%) via both glomerular filtration and active transport, biliary excretion <10%, significant inter- and inpatient variability; small amounts are excreted in the feces

Urine: 44%-100% excreted unchanged

Cl- low dose: 36-138 mL/min/m²; high dose: 24-100 mL/min/m²; clearance higher in children than in adults

t_{1/2} - low doses: 3-10 hours; high doses: 8-12 hours

t_{1/2} β - 8-15 hours

IV COMPATIBILITY

normal saline, dextrose 5%, lactated Ringer's

ROUTES

oral (well absorbed <30 mg/m²)
intramuscular (rotate sites)
direct IV (low doses 25-40 mg/m²/week)
intermittent IV (in appropriate volume over 1-8 hours)
continuous IV (in appropriate volume over 24 hours)
intrathecal (preservative-free only)

EXTRAVASATION HAZARD

minimal

ANTIEMETIC RISK

LOW RISK (Less than 10% of patients)

- No routine antiemetic pre-chemotherapy or post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

Continued Next Page...

METHOTREXATE

ADMINISTRATION

- Doses <100mg may be given by slow push through sidearm of free flowing IV (5% Dextrose, Normal Saline) over 1-2 minutes; may give by push over 15 minutes for larger doses (eg. 100-300mg) (*administering nurse should be certified to administer IV push chemotherapy agents*)
- May be given by IM or direct IV push, followed by a Normal Saline IV flush, if no IV line has been set up
- Larger doses (eg. >100mg) may be followed by Leucovorin rescue 24 hours later
- Doses from 100-200mg may be mixed in 100mL minibag (5% Dextrose, Normal Saline); Infuse over 30 (to 60) minutes
- Doses from 200-500mg may be mixed in 250-500mL bag (5% Dextrose, Normal Saline); Infuse over 30 (to 120) minutes
- Doses from >500mg may be mixed in 500mL bag (5% Dextrose, Normal Saline); Infuse over 1 (to 4) hour(s)

High-Dose (>1g/m²)

- Hydrate with Normal Saline at 100-125mL/hour, starting 6 to 12 hours before Methotrexate; measure urine output (>60 mL/hour)
- Alkalinize urine, starting 6-12 hours before Methotrexate, with Sodium Bicarbonate 50mmol in alternating litres of IV hydration fluid (or in each litre); maintain urine pH > 7.0 (may also give Sodium Bicarbonate 1000mg/m² PO q6h or Acetazolamide 250 to 500mg PO q6h)
- Admix into 1000mL (5% Dextrose, Normal Saline) and infuse over 4 hours, as an inpatient
- Continue hydration and alkalinization for 24 hours after completion of Methotrexate infusion
- Leucovorin rescue to start 24 hours after Methotrexate dosing finished; continue until serum levels drop below toxic range (<0.05µmol/L)

Intrathecal

- Reconstitute powder with preservative-free 0.9% Sodium Chloride, or use preservative-free solution, use solution immediately

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Clinical assessment of stomatitis:** oral examination upon patient complaint of a sore mouth
- **Baseline renal function tests** (if failure suspected) [serum creatinine, electrolytes & BUN]

SUGGESTED CRITERIA

- Baseline and periodic **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- Baseline and periodic **chest X-ray**

SIGNIFICANT INTERACTIONS

alcohol & other hepatotoxic agents, amiodarone, antibiotics, anticonvulsant agents, asparaginase, co-trimoxazole, cyclosporin, etretinate, leucovorin, nitrous oxide, non-steroidal anti-inflammatory drugs (NSAIDs), non-absorbable oral antibiotics, phenytoin, probenecid, theophylline, thiazide diuretics, thiopurines (azathioprine, mercaptopurine), warfarin other antineoplastic agents

METHOTREXATE

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)

- * anaphylaxis (rare)
- nausea and vomiting** (dose related, 40% with high dose)
- allergic (fever and chills, rare) radiation recall reaction (rare)
- chemical meningitis (intrathecal use)
- lung problems (pulmonary edema, pleuritic chest pain)

EARLY ONSET (days to weeks)

- * **low WBC, RBC, platelets** (**myelosuppression**, nadir 7-14 days, recovery 14-21 days)
- mouth sores** (dose related, stomatitis)
- * **gastrointestinal problems** (diarrhea, bleeding, perforation)
- liver problems (elevated liver function tests)
- skin problems (pigmentation changes, photosensitivity, rash)
- loss of appetite (anorexia), hair loss (alopecia, usually mild)
- lung problems (interstitial pneumonitis)
- eye problems (conjunctivitis), CNS problems (acute encephalopathy)
- blood problems (megaloblastosis)
- kidney problems (toxic neuropathy, with high doses)

DELAYED/LATE ONSET (weeks- years)

- liver problems (fibrosis, cirrhosis)
- central nervous system problems

Intrathecal Methotrexate

IMMEDIATE ONSET (hours to days)

- acute chemical arachnoiditis (transient headache, back pain, nuchal rigidity)
- mild fever

EARLY ONSET (days to weeks)

- * CNS toxicity (subacute myelopathy [paraparesis, paralysis of spinal nerve roots], chronic leukoencephalopathy [may be progressive and fatal-confusion, irritability, somnolence, ataxia, dementia, seizures, coma], increased CSF pressure)- all rare; may be associated with combinations which include IV chemotherapy and radiotherapy)

INDICATIONS AND OTHER USES

- Acute lymphocytic leukemia
- Choriocarcinoma
- Graft versus host disease (prophylaxis)
- Mycosis fungoides
- Non-Hodgkin's lymphoma

OTHER ONCOLOGY USES

- Breast cancer*
- Bladder cancer*
- Chorioadenoma destruens and hydatidiform mole*
- Head and neck cancer*
- Lung cancer*
- Meningeal leukemia*
- Osteogenic sarcoma*
- Sarcoma, adult soft tissue*
- Prevention of acute graft-versus host disease*

CONTRAINDICATIONS

- pregnancy and breast feeding
- low WBC, RBC, platelets (myelosuppression)
- effusions
- severe renal failure

METHOTREXATE

DOSING

Oral:

- daily: 0.625-2.5 mg/kg
- q1-2w: 15-30 mg x 5 days (or IM)
- biw (twice a week): 10-15 mg/m²/dose (or IM)
- q2w: 2.5 mg/kg
- daily: 3.3 mg/m² x 4-6 weeks

Intravenous:

- q1w: 25-40 mg/m²
- q1-3w: 100 mg-30 g/m² followed by leucovorin rescue within 2-24 hours
- 1 mg/kg IM/IV days 1, 3, 5, 7 (with leucovorin calcium 10% of MTX dose IM days 2, 4, 6, 8)- Gestational trophoblastic disease
- 0.4 mg/kg/day IV daily for 5 days- Gestational trophoblastic disease
- 15mg/m² (IBSA) on Day +1 and 10 mg/m² on days +3, +6, and +11- BMT graft-versus-host-disease prophylaxis
- q4w: 40 mg/m² days 1 and 8
- q4w: 30 mg/m² days 1, 15 and 22
- 220 mg/m² IV bolus followed by 60 mg/m²/hour x 36 hours by continuous IV infusion - Acute lymphoblastic leukemia

Intrathecal:

- q4-7d: 12 mg in 6 mL preservative-free NS
- Dose is the same whether given intrathecally or into an Ommaya (intraventricular) reservoir. Elderly patients may require a reduced dose.

Leucovorin rescue:

- See leucovorin monograph for dosing guidelines for leucovorin rescue.

Pediatric

Oral:

- q1w: 15-20 mg/m²

Intravenous:

- q4w: 300-3000 mg/m²
- q3-4w: 8-12 g/m² IV (top dose 20 g) with hydration of 3 L/m²/day, alkalinization of urine and leucovorin rescue; use only preservative-free methotrexate
- 6 g/m² loading dose, followed by 1.2 g/m²/hour x 23 hours with leucovorin rescue starting 12 hours after end of methotrexate infusion;
- 200 mg/m² loading dose, followed by 12 mg/m² q3h x 6 doses, then q6h until methotrexate levels fall below 0.1 μmol; use preservative-free methotrexate

Intrathecal:

- <1 year 6 mg
- 1-2 year 8 mg
- 2-3 year 10 mg
- >3 year 12 mg
- Dose of methotrexate is the same whether it is given intrathecally or into an Ommaya (intraventricular) reservoir.

Other dosing may be indicated in specific regimens

DOSE ADJUSTMENT CRITERIA

Hepatic dysfunction

1. If Bili = 50-85 μmol/L or AST > 180 IU/L, REDUCE to **75%** dose

2. If Bili > 85 μmol/L, **Omit** dose

Renal failure (Suggested action)

1. If CrCl = 0.2-0.8 mL/sec or Serum Creatinine = 100-180 μmol/L, REDUCE to **50%** dose
2. If CrCl < 0.2 mL/sec or Serum Creatinine > 180 μmol/L, **Omit** dose

METHOTREXATE

PHARMACEUTICAL CONSIDERATIONS

Tablets: 2.5 mg. The Lederle brand also contains cornstarch, magnesium stearate and lactose but is dye- and tartrazine-free. The David Bull Laboratories product contains no preservatives or colouring agents. Store at room temperature.

Injection

20 mg powder, 2.5 mg/mL solution (preservative-free), 10 mg/mL solution (preservative-free), and 25 mg/mL solution (preservative-free or preserved with benzyl alcohol). Store at room temperature, protected from light.

Reconstitute 20 mg powder with 2-10 mL NS, D5W or SWI to desired concentration.

For intrathecal administration, reconstitute 20 mg vial of powder with 10 or 20 mL preservative-free NS, Elliott's B solution or the patient's own spinal fluid to a final concentration of 2 or 1 mg/mL, respectively. Prepare immediately before use.

Reconstituted solution for injection

Stable at least 1 week at room temperature protected from light. However, the manufacturers recommend reconstitution immediately before use and that unused portions of vials reconstituted with preservative-free diluents be discarded.

Stability in syringes

A 50 mg/mL solution is reportedly stable for at least 70 days at 25° C in plastic syringes. Cheung reported that mixtures of methotrexate 12 mg, cytarabine 30 or 50 mg, and hydrocortisone sodium succinate 15 or 25 mg in 12 mL of NS, D5W, Ringer's injection or lactated Ringer's were found to be physically compatible in disposable syringes at 25°C for at least 10 hours.

Diluted solution for infusion

Compatible for 7 days at room temperature in NS, D5W, D10W, dextrose-saline combinations, Ringer's Injection, lactated Ringer's, and 5% sodium bicarbonate. Solutions of 0.1 mg/mL are reported to undergo photodegradation (5-8% loss in 10 days, 11-17% in 20 days) on exposure to light. This effect was not noted in the more concentrated solutions.

Immersion of a needle with an aluminum component in methotrexate 25 mg/mL resulted in the formation of orange crystals on the aluminum surface after 36 hours at room temperature, protected from light.

Some mixtures with cytarabine, hydrocortisone sodium succinate, and sodium bicarbonate are compatible (see Stability in Syringes). Compatible with ondansetron. It is recommended that methotrexate not be mixed with other drugs. Incompatible with bleomycin, prednisolone sodium phosphate, ranitidine and some concentrations of heparin and metoclopramide.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-

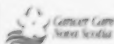
Injection- Basic Level for low dose, Specialized Level (Capital Health Only) for high-dose; Advanced Level for intrathecal doses

Oral- Basic Level for ordering on preprinted Physician Standing Order

CDHA Status Formulary

Pharmacare Status Formulary

NOTE: It is recommended to limit ordering of this medication to preprinted Physician Standing Order form, for patient safety



METOCLOPRAMIDE

(Dopaminergic blocking Agent, Antiemetic)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Maxeran®

Tablets with 10mg Metoclopramide

Generic products available

Vials with 10mg/2mL, 500mg/25mL

MECHANISM OF ACTION

Blocks dopamine receptors and (in high doses) serotonin receptors in the chemoreceptor trigger zone of the CNS and GI tract; enhances the response to acetylcholine of tissue in upper GI tract causing enhanced motility and accelerated gastric emptying without stimulating gastric, biliary, or pancreatic secretions.

PHARMACOKINETICS

Oral Absorption

Bioavailability: 66% to 80%

Distribution

enters breast-milk, crosses the placenta
cross blood brain barrier? Yes

Vd- 2-4 L/kgPPB- 30-40%, primarily
to α -acid-glycoprotein

Metabolism

in the liver, major metabolites are
glucuronide, metoclopramide sulfate,
and 2-[(4-amino-5-chloro-2-
methoxybenzoyl)-amino]acetic acid

Excretion

70 to 85% in the urine, primarily as
unchanged drug (~19%); 2% to 3.3%
in the feces.

Urine: 85% within 72 hours as
unchanged drug and sulfate and
glucuronide conjugates
 $t_{1/2}$ - 4-7 hours (may be dose-dependent)

IV COMPATIBILITY

5% Dextrose, normal saline

ROUTES

orally

I V: direct push, short (15-30 min) or
continuous infusion

I M

Continuous S C infusion
rectal

ADMINISTRATION

- Mix in 50mL minibag (5% Dextrose, Normal Saline). Give over 15-60 minutes
- Doses of 20mg or less may be given as direct IV or through side arm of a free-flowing IV, over 1 to 2 minutes, followed by a flush with Normal Saline
- May be admixed with Dexamethasone in same minibag

EXTRAVASATION HAZARD

no

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

EARLY ONSET

(days to weeks)

DELAYED/LATE ONSET

drowsiness, restlessness

rare: rash

extrapyramidal reactions (34%)

* methemoglobinemia

diarrhea, weakness

rare: insomnia, depression

INDICATIONS AND OTHER USES

- Prevention of nausea and vomiting induced by chemotherapy or radiotherapy
- Management of delayed gastric emptying (promotility agent)

SIGNIFICANT INTERACTIONS

other anticholinergic agents
opiates and other CNS depressants

Continued Next Page...

METOCLOPRAMIDE

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Observe for signs of **tardive dyskinesia** and other movement disorders
- Periodic monitoring of **renal function** [serum creatinine, electrolytes & BUN]
- In diabetic patients, monitor **serum glucose**

SUGGESTED CRITERIA

- Baseline **ophthalmological exam** (check for glaucoma)
- Periodic **renal function tests** [serum creatinine, electrolytes & BUN], on repeat doses

INVOLUNTARY MOVEMENT

- 0 None
- 1 Mild agitation, restlessness
- 2 Moderate agitation
- 3 Torticollis, oculogyric crisis, severe agitation

Rated at each clinic visit or in response to patient complaint

DOSING

Injection (antiemetic for highly emetogenic chemotherapy)

- 1-2mg/Kg IV over 15 minutes, starting 30 minutes before chemotherapy; repeat every 3 hours for 3 doses if emesis not controlled
- Administer diphenhydramine 25-50mg IV/po before metoclopramide to prevent extrapyramidal reactions
- Largely replaced by serotonin receptor antagonists for highly emetogenic chemotherapy
- May be given as 60-120mg/24hr continuous SC infusion for refractory cases of chronic nausea
- **Oral:**
- 10-20mg po before chemotherapy or radiotherapy (may include diphenhydramine 25-50mg po for prophylaxis)- rarely used pre-chemotherapy
- 10-20mg po q4h after chemotherapy (regular dosing or PRN dosing); usually given along with dexamethasone 4-8mg po)- may be used for delayed nausea or vomiting
- 10mg po/SC q4h + 10mg po/SC PRN for rescue- first-line treatment of chronic nausea alone or with dexamethasone 10mg po/SC bid

Pediatric

Other dosing may be indicated

Injection

- 1-2mg/Kg IV over 15 minutes, starting 30 minutes before chemotherapy; repeat every 2-4 hours

DOSE ADJUSTMENT CRITERIA

Renal failure may be associated with increased extrapyramidal effects; dose reduction may be required

CONTRAINDICATIONS

- hypersensitivity to metoclopramide or any component
- GI obstruction, perforation or hemorrhage
- pheochromocytoma
- history of seizure disorder;
- Parkinson's disease
- mental illness
- renal impairment
- extrapyramidal reactions

Continued Next Page...

METOCLOPRAMIDE**PHARMACEUTICAL CONSIDERATIONS**

Tablets: 10mg metoclopramide, white tablets.

Injection: 5mg/mL solution for injection- multiple vial sizes, including 10mg/2mL, 50mg/10mL & 100mg/50mL. Store at room temperature; protect from freezing. Protect from light.

Doses up to 10mg/2mL may be given as IV push over 1-2 minutes

Diluted solution for infusion

Dilute doses of 10-150mg in 50mL D5W or NS. Diluted solution stable at room temperature or refrigeration for up to 24 hours. Light protection not required for diluted solutions if used within 24 hours.

Compatible with diphenhydramine.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-

Injection-Basic Level.

Oral- Take Home Prescription

CDHA Status Formulary

Pharmacare Status Formulary

MITOMYCIN

(Antineoplastic Agent, Antibiotic)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Mutamycin® Vials with 5mg, 20mg for reconstitution

Generic products available

MECHANISM OF ACTION

Mitomycin acts like an alkylating agent, inducing DNA cross-linking, primarily with guanine and cytosine pairs. Inhibits DNA synthesis, degrades preformed DNA, causes nuclear lysis and formation of giant cells. While not phase-specific per se, it has its maximum effect against cells in late G1 and early S phase.

PHARMACOKINETICS

Oral Absorption

erratic

Distribution

detectable levels in kidney, muscles, heart, lungs, intestine and stomach, found in ascites, enters breast-milk cross blood brain barrier? no

Vd- 22-25 L/m² PPB- no information

Metabolism

prodrug activated in vivo, primary means of elimination is by hepatic metabolism metabolite(s): active, inactive- yes

Excretion

excreted in urine, detected in bile and feces, biliary level may exceed plasma level

Urine: <10% as unchanged drug
t_{1/2} α - 23-78 minutes t_{1/2} β - 48 minutes
Cl- 201-810 mL/min/m²

IV COMPATIBILITY

normal saline (preferred), dextrose 5% (limited stability), lactated Ringer's

ROUTES

direct IV (preferred)
intermittent IV (in 50-100 mL over 20-30 minutes)
intravesical (dwell time 2 hours)

ADMINISTRATION

- Slow push through sidearm of free flowing IV (Normal Saline). Give 1 5mg/3mL per minute (*administering nurse should be certified to administer IV push chemotherapy agents*)
- Doses may be mixed in 50-100mL minibag (Normal Saline); Infuse through sidearm of free flowing IV over 10-30 minutes

INDICATIONS AND OTHER USES

- Bladder cancer
- Gastric cancer
- Colorectal cancer

OTHER ONCOLOGY USES

Breast cancer

Cervical cancer

Head and neck cancer

Lung cancer, non-small cell

Ovarian cancer

Pancreatic cancer

Primary unknown cancer

Osteogenic sarcoma

EXTRAVASATION HAZARD

VESICANT (tissue damage on extravasation)

Management- stop IV, aspirate, elevate limb, cold intermittent compresses
Follow Extravasation Guidelines

ANTIEMETIC RISK

INTERMEDIATE RISK (10-30% of patients)

- Use a dexamethasone pre-chemotherapy and a dopamine receptor antagonist PRN post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

CONTRAINDICATIONS

- pregnancy and breast feeding
- low WBC, RBC, platelets (myelosuppression)

SIGNIFICANT INTERACTIONS

dicoumarol, doxorubicin, gemcitabine, medroxyprogesterone, pyridoxine, vinca alkaloid

Continued Next Page...

MITOMYCIN

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

- fever
- vein irritation (phlebitis)
- bladder irritation** (cystitis with bladder instillation)
- nausea and vomiting (usually mild, onset 1-2 hours, nausea may last 2-3 days)
- * acute bronchospasm (rare- within 4-12 hours after IV therapy)

DELAYED/LATE ONSET (weeks- years)

- * lung problems (chronic fibrosis)
- * kidney problems (renal failure and microangiopathic hemolytic anemia)
- central nervous system problems (rare, acute encephalopathy)

EARLY ONSET (days to weeks)

- * **low WBC, RBC, platelets** (**myelosuppression**, nadir 24-28 days, recovery 42-56 days, myelosuppression may be cumulative)
- lung problems (interstitial pneumonitis)
- mouth sores (usually mild, stomatitis)
- liver problems (elevated liver function tests)
- hair loss (rare, alopecia)
- skin problems (rash, blue bands in nails)
- central nervous system problems (rare, acute encephalopathy)
- blurred vision; menstrual problems (amenorrhea)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Clinical pulmonary exam**, including auscultation, pulmonary toxicity ratings (Cough, SOB)
- **Baseline & periodic renal function tests** (if failure suspected) [serum creatinine, electrolytes & BUN]

SHORT OF BREATH

- 0 No change
- 1 Abnormal PFT's
- 2 Dyspnea on exertion
- 3 Dyspnea at normal level of activity
- 4 Dyspnea at rest

COUGH

- 0 None
- 1 Mild
- 2 Moderate
- 3 Severe

Rated At Each Clinic Visit

SUGGESTED CRITERIA

- **Blood pressure** at each visit
- **Baseline liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- **Baseline and periodic chest X-ray**
- **Local Site Toxicity ratings**, if incident of phlebitis
- **Neurological toxicity (Lethargy)** if patient complaint of symptoms

LETHARGY

- 0 None
- 1 Mild (Performance Status [PS] decreased by 1)
- 2 Moderate (PS decreased by 2)
- 3 Severe (PS decreased by 3)

LOCAL SITE TOXICITY

- 0 None
- 1 Pain
- 2 Pain & inflammation; phlebitis
- 3 Ulceration
- 4 Plastic surgery

Upon Patient Complaint Or Clinical Event

MITOMYCIN

DOSING

Intravenous:

- q6-8w: 10-20 mg/m²
- q6-8w: 2 mg/m²/day x 5 days, stop x 2 days, repeat x 1

Intravesical:

- q1w: 30-60 mg in 20-60 ml SWI x 6 then monthly x 1 year

Pediatric: No pediatric indications

Myelosuppression, particularly anemia can be cumulative. This can be minimized by keeping total lifetime doses under 50-60 mg/m²

Other dosing may be indicated

DOSE ADJUSTMENT CRITERIA

Hepatic dysfunction

If Bili = 50-85 µmol/L or AST > 180 IU/L,
REDUCE to 75% dose

Renal failure (Suggested action)

If CrCl < 0.2 mL/sec, REDUCE to 75% dose

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Intermediate Level

CDHA Status Formulary

Pharmacare Status Formulary (red)

PHARMACEUTICAL CONSIDERATIONS

Injection

5 mg, 20 mg; also contains mannitol. Store at room temperature. Protect from light. Reconstitute powder with SWI to a final concentration of 0.5 mg/mL; allow to stand at room temperature or shake vial under warm tap water for 2 minutes to assist dissolution. If reconstituted to a final concentration of 1 mg/mL, the solution should not be refrigerated because of the risk of crystal formation. May also be reconstituted to a final concentration of 2 mg/mL.

Reconstituted solution for injection

Clear blue or purple solution. Stable for 7 days at room temperature (up to 30°C) and for 14 days when refrigerated. Protect from light if not used within 24 hours. Solutions reconstituted to 1 mg/mL undergo 6% loss in 24 hours at 21-25°C and may precipitate within 4 days.

Diluted solution for infusion

Varying stability is reported. The manufacturer reports compatibility with D5W, NS and sodium lactate injection for 3, 12 and 24 hours respectively, at concentrations of 20-40 mcg/mL and stored at room temperature. King reports 24 hours stability in NS in glass or plastic containers but only 1 or 2 hours in D5W in glass or PVC containers, respectively.

Filtration of 10-75 mcg/mL solutions through cellulose nitrate/cellulose acetate ester (Millex OR) or Teflon (Millex FG) filters resulted in little or no loss of mitomycin. Compatible with ondansetron. It is recommended that mitomycin not be mixed with other drugs.



MITOXANTRONE

(Antineoplastic Agent; Anthracenedione)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Novantrone® Vials with 20mg/10mL, 25mg/12.5mL

MECHANISM OF ACTION

An analogue of the anthracyclines, mitoxantrone intercalates DNA; binds to nucleic acids and inhibits DNA and RNA synthesis by template disordering and steric obstruction; replication is decreased by binding to DNA topoisomerase 2; mitoxantrone also seems to inhibit the incorporation of uridine into RNA and thymidine into DNA

PHARMACOKINETICS

Oral Absorption

poor

Distribution

highest concentration in pleural fluid, kidney, thyroid, liver, heart and red blood cells; enters breast- milk
cross blood brain barrier? no information
Vd- 14 L/kg

PPB >95% Protein; 78% (albumin)

Metabolism

in liver to polar compounds
metabolite(s): active- no; inactive- yes

Excretion

mainly in bile (18% in feces within 5 days), small amount in urine

Urine: 10% within 5 days

$t_{1/2} \alpha$ - 0.14 hours $t_{1/2} \beta$ - 3.1 hours

$t_{1/2} \gamma$ - 36-215 hours

Cl- 217-600 mL/min/m²

IV COMPATIBILITY

normal saline, dextrose 5%

ROUTES

direct IV (preferred)
intermittent IV (over 10-15 minutes)
continuous IV (investigational)
intrathecal (safety not established)
intraperitoneal, intra-arterial, intravesical

ADMINISTRATION

- Slow push through sidearm of free flowing IV over a period of not less than 3-5 minutes. May give 4mg/2mL per minute (*administering nurse should be certified to administer IV push chemotherapy agents*)
- Mix in 50-100mL bag (Normal Saline or 5% Dextrose); Infuse over 10-15 minutes through free-flowing IV

INDICATIONS AND OTHER USES

- Acute lymphocytic leukemia
- Acute myelogenous leukemia
- Acute non-lymphocytic leukemia
- Breast cancer
- Non-Hodgkin's lymphoma

OTHER ONCOLOGY USES

Chronic myelogenous leukemia

Gastric cancer

Liver cancer

Ovarian cancer

Prostate cancer

EXTRAVASATION HAZARD

Nonvesicant; blue discolouration of skin which slowly fades

Management- stop IV, aspirate, elevate limb, cold intermittent compresses

Follow Extravasation Guidelines

CONTRAINDICATIONS

- known hypersensitivity to mitoxantrone or other anthracyclines
- pregnancy and breast feeding
- low WBC, RBC, platelets (myelosuppression)
- cardiovascular disease (including hypertension, angina, arrhythmias)

SIGNIFICANT INTERACTIONS

acetylcysteine, heparin

Continued Next Page...

MITOXANTRONE

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)

- * anaphylaxis (rare)
- nausea and vomiting** (30%, severe 3.5%)
- urine discolouration** (blue-green, lasts 24 hours)
- injection site problems (phlebitis 10%, vein discolouration)

DELAYED/LATE ONSET

- heart problems (transient arrhythmias, congestive heart failure, cardiomyopathy)
- kidney problems (renal damage, rare)

EARLY ONSET (days to weeks)

- * **low WBC, RBC, platelets** (**myelosuppression**, nadir 10 days, recovery 21 days)
- mouth sores** (stomatitis)
- hair loss (alopecia, 15%, severe 1%)
- gastrointestinal problems (diarrhea, anorexia)
- liver problems (elevated liver function tests)
- heart problems (transient arrhythmias, congestive heart failure, cardiomyopathy)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC) and serum uric acid levels** before each cycle of treatment
- Clinical exam for symptoms of **Congestive Heart Failure**
- Periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels
- Baseline **liver function tests** (especially if poor Performance Status) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]

SUGGESTED CRITERIA

- Baseline **cardiac function tests** (Echo, RNA and/or MUGA scans) for all patients with cardiac risk factors

CARDIAC

0. None
1. —
2. Asymptomatic, resting ejection fraction decline by >10% baseline; or abnormal cardiac function tests (LVEF >50) with no baseline for comparison
3. Mild Congestive Heart Failure, responds to therapy
4. Severe/refractory Congestive Heart Failure

At cumulative dose threshold and subsequent intervals

For Cardiac Toxicity Ratings:

First rating at the Mitoxantrone cumulative dose **threshold** of **160mg/m²**, & repeat ratings at each cumulative dose **increment** of **30mg/m²** above threshold (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation)

Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

ANTIEMETIC RISK

INTERMEDIATE RISK (10-30% of patients)

- Use a dexamethasone pre-chemotherapy and a dopamine receptor antagonist PRN post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

MITOXANTRONE

DOSING

Intravenous:

- q3w: 12-14 mg/m²
- decrease by 2-4 mg/m² for combination therapy, prior therapy, or poor general condition
- 12 mg/m²/day IV x 5 days for 1-2 cycles

Maximum lifetime dose:

- 140-160 mg/m² (no prior anthracycline, normal cardiac function, less in children)
- 120 mg/m² (in combination with previous anthracycline, thoracic radiation or cyclophosphamide)
- 100 mg/m² (previous maximum dose anthracycline, if cardiac assessment acceptable)

- Careful cardiac monitoring is important as cardiotoxicity may occasionally occur at lower cumulative doses. If tumour responding when lifetime dose reached, obtain cardiac consultation before continuing treatment.

Bone marrow transplant:

- much higher doses are used for tumour ablation prior to marrow transplant than for standard treatment regimens, eg, 12 mg/m²/day IV x 3 days or 60-75 mg/m² IV in multiday, divided doses; in combination with other cytotoxic chemotherapy

Pediatric

Intravenous:

q3-4w: 8 mg/m²/day IV x 5 days

Other dosing may be indicated in specific regimens

DOSE ADJUSTMENT CRITERIA

Hepatic dysfunction: (Suggested action)

If Bili > 50µmol/L, REDUCE to 50% dose

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Intermediate Level

CDHA Status

Formulary

Pharmacare Status Formulary (red)

PHARMACEUTICAL CONSIDERATIONS

Injection

2 mg/mL clear, dark blue solution in 10 mL and 12.5 mL vials. Preservative- and tartrazine-free. Also contains acetic acid, sodium acetate, sodium chloride and sodium sulfate (from sodium metabisulfite). Store at room temperature. Refrigeration may result in a precipitate which redissolves after warming to room temperature. Do not freeze. The manufacturer recommends that unused portions of a vial be discarded, although Walker et al reported less than 10% loss of initial concentration in partial vials stored at 4 and 23°C for 42 days.

Diluted solution for infusion

Compatible with D5W or NS. The manufacturer recommends that diluted solutions be stored at room temperature and used within 24 hours; however, dilutions of 20-500 mcg/mL are reported to be stable for at least 48 hours in NS, D5W or D5NS in PVC containers, refrigerated or stored at room temperature. Do not freeze.

Stability in syringes

Walker et al reported less than 10% loss of initial mitoxantrone concentration when a 2 mg/mL solution was stored in PVC (Monoject) syringes at 4 and 23°C for 42 days.

Filtration

Mitoxantrone potency is not lost when filtered through 0.2 micron Millipore filters. Compatible with ondansetron. Some mixtures with hydrocortisone in NS are reported to be compatible for 24 hours. It is recommended that mitoxantrone not be mixed with other drugs. Physically incompatible with heparin (precipitate formation).

NILUTAMIDE

(Antineoplastic Agent; Antiandrogen)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Anandron®

Tablets with 50mg, 100mg Nilutamide

MECHANISM OF ACTION

Nilutamide acts as an antiandrogen by inhibiting androgen uptake and/or inhibiting nuclear binding of androgen in target tissues. It specifically blocks the action of androgens by interacting with cytosolic androgen receptor F sites in the target tissues.

PHARMACOKINETICS

Oral Absorption

yes, rapidly and completely

Distribution

no information

cross blood brain barrier? no information

Vd- no information

PPB- 80%-84% to plasma proteins, some binding to erythrocytes

Metabolism

liver, involves hepatic microsomal enzyme oxidation system

metabolite(s): active, inactive- yes

Excretion

mainly in urine as metabolites (67% to 78%); hepatic: 1% to 7%; 1.4-7% in feces within 4-6 days

Urine: 67%-78%, <2% unchanged

t½ mean: 50 hours (range: 23-87 hours)

ROUTES

oral

DOSING

Oral:

- daily: 150-300 mg

- tid: 100 mg

Pediatric: No pediatric indications

INDICATIONS AND OTHER USES

- Prostate cancer

CONTRAINDICATIONS

- known hypersensitivity to nilutamide
- severe low RBC (anemia)
- severe liver failure

SIGNIFICANT INTERACTIONS

alcohol, diazepam, lidocaine, phenytoin, propranolol, theophylline, warfarin

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

nausea, vomiting (10-30%, mild, transient)

DELAYED/LATE ONSET (weeks- years)

liver problems (rare, hepatitis)
lung problems (rare, interstitial lung disease)

EARLY ONSET (days to weeks)

vision problems (27%, light-to-dark adaptation and colour perception)

breast swelling or soreness (4-44%, gynecomastia)

hot flushes (28-77%)

nausea, vomiting (10-30%, mild, transient)

liver problems (8%, elevated liver function tests, transient)

gastrointestinal problems (constipation, gastric pain)

blood problems (4%, anemia)

lung problems (6%, dyspnea)

dizziness

fatigue

Continued Next Page...

NILUTAMIDE

CLINICAL MONITORING

RECOMMENDED CRITERIA

NO RECOMMENDED TOXICITY RATINGS

SUGGESTED CRITERIA

- Periodic **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]

DOSE ADJUSTMENT CRITERIA

Hepatic failure

STOP if AST or ALT > 105IU/L
(*Suggested action*)

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level: Take Home
Prescription (NOTE: Use of pre-
printed Physician Standing Order is
recommended)

CDHA Status	Non-Formulary
Pharmacare Status	Formulary

OCTREOTIDE

(Antisecretory Agent: Somatostatin Analog)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Sandostatin® Ampuls with 50, g/mL, 100, g/mL, 500, g/mL
Multidose vials with 1000, g/5mL
Sandostatin LAR® Vials with 10mg, 20mg, 30mg for dilution with 2mL
vehicle for dilution (ampuls included)

MECHANISM OF ACTION

Mimics natural somatostatin by inhibiting serotonin release, and the secretion of gastrin, VIP, insulin, glucagon, secretin, motilin, and pancreatic polypeptide

PHARMACOKINETICS

Oral Absorption

absorbed but still under study

Distribution

enters breast-milk

cross blood brain barrier? no information

Vd- 14 L PPB- 65% to lipoprotein

Metabolism

extensive by the liver; slowly catabolized
to inactive fragments

metabolite(s): active- no information
inactive- yes

Excretion

mainly by kidneys

Urine: 32% is excreted unchanged

$t_{1/2} \alpha$ - SC: 1.7 hours

$t_{1/2} \beta$ - IV: 10 minutes

$t_{1/2} \gamma$ - IV: 1.5 hours

Cl- 160 mL/min;

impaired renal function: 75 mL/min

IV COMPATIBILITY

normal saline

ROUTES

subcutaneous (preferred, rotate sites,
can give continuous)

direct IV (emergency situations)

continuous infusion (emergency
situations)

intrathecal (continuous infusion for
pain control)

ADMINISTRATION

- Subcutaneous self-administration (or
administered by home caregiver)

EXTRAVASATION HAZARD

none

SIGNIFICANT INTERACTIONS

diazoxide, sulfonylureas, beta blockers,
insulin, oral cyclosporine

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)

nausea (9%), vomiting (3%)

pain at injection site (8%), redness,
swelling

diarrhea (7%), loose stools
(3%), constipation (1%)

DELAYED/LATE ONSET (weeks- years)

gallstones (<1%)

EARLY ONSET (days to weeks)

blood glucose problems (<1%,

hyperglycemia, hypoglycemia)

hair loss (1%, alopecia)

gastrointestinal problems (abdominal
pain 4%, steatorrhea 4%)

CNS problems (headache 2%,
dizziness 2%, fatigue 1%,
weakness 1%)

heart problems (1%, edema)

liver problems (jaundice, elevated liver
function tests, rare)



OCTREOTIDE

DOSING

Subcutaneous:

Daily:

- start at 50 mcg SC once or twice daily; titrate dose for maintenance based on response (eg, 150 mcg [range 50-2000 mcg20] SC three times daily)
- starting dose may be higher depending on severity of symptoms
- acromegaly maximum dose: 1500 mcg per day

PRN:

- 100 mcg SC for 2 doses, 15 min and 6 h after chemotherapy

Intramuscular:

4 weeks:

- octreotide LAR: 20 mg (range 10-40 mg) IM for one dose on day 1
- can be started the day after the last dose of octreotide SC.
- carcinoid tumours and VIPomas: Continue octreotide SC for at least two weeks in the same dose as before the switch. Some patients may require 3-4 weeks of such therapy.
- 10 mg starting dose not recommended as therapeutic levels reached more rapidly with a 20 mg dose
- For exacerbation of symptoms, give octreotide SC for a few days at the same dose as prior to switch to octreotide LAR. When symptoms are controlled, octreotide SC can be discontinued.

Intravenous:

Stat: 50 mcg IV, may repeat in 15 seconds

Adequate trial:

- acromegaly: 3 months4
- carcinoid tumours and VIPomas: octreotide SC: at least 2 weeks, then switch "responders" to octreotide LAR

Pediatric: No pediatric indications

Other dosing may be indicated

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Baseline and periodic **serum glucose levels**, especially in diabetic patients
- **Ultrasonograph of the gall bladder**, to assess the presence of gallstones (during long-term therapy)

SUGGESTED CRITERIA

- Baseline and periodic **thyroid function tests**

INDICATIONS AND OTHER USES

- Acromegaly
- Carcinoid syndrome
- VIPomas

OTHER ONCOLOGY USES

Chemotherapy-induced diarrhea
Malignant intestinal obstruction
Pancreatic cancer
Gastro-entero pancreatic (GEP)
endocrine tumours
Thymoma

CONTRAINDICATIONS

- known hypersensitivity to octreotide
- pregnancy and breast feeding

OCTREOTIDE

PHARMACEUTICAL CONSIDERATIONS

Injection:

50 mcg/mL, 100 mcg/mL or 500 mcg/mL of SC octreotide ampules; 200 mcg/mL (5 mL vial) of SC octreotide multidose vials; 10 mg, 20 mg or 30 mg of octreotide LAR vials with two vehicle ampules. For prolonged storage, keep under refrigeration. Avoid freezing of SC multidose vials. For day-to-day use, ampules and SC multidose vials may be stored at room temperature for up to 2 weeks. LAR vials can remain at room temperature on the day of injection but the suspension should be prepared immediately before administration. Do not use heat to bring solution rapidly to room temperature, as octreotide may be damaged. Protect from light. Discard unused portion of SC ampules.

Reconstitute octreotide LAR powder:

Allow octreotide LAR and vehicle vials to warm at room temperature for 30-60 minutes. Suspend powder with 2 mL of vehicle immediately before injection. Each kit contains a reserve vehicle ampule. Without disturbing the powder, gently inject the vehicle into the vial by running the it down the inside wall of the vial. Withdraw any excess air from the vial. Do not disturb the vial until the vehicle has wetted the powder. Once complete wetting has occurred (about 2-5 minutes), the vial should be moderately swirled until a uniform suspension is achieved. Do not shake the vial vigorously. Slowly withdraw the entire vial contents into the syringe. Immediately change the needle (supplied). Gently invert the syringe as needed to maintain a uniform suspension.

Reconstituted octreotide LAR suspension for injection: should be injected immediately.

Diluted solution for infusion:

For continuous IV infusion, dilute octreotide SC solution in NS. Stable for 24 hours at room temperature. Discard unused portion. Reconstituted octreotide LAR suspension must never be given IV.

Syringe stability:

One study reported that octreotide retained its potency for 30 days when stored in Travenol, Minimed and Becton-Dickinson (Plastipak) plastic syringes of polypropylene and natural rubber. Another study, using Becton-Dickinson tip caps and polypropylene syringes, recommended a maximum storage time of one week at room temperature, whether protected from light or not. A third study, using Terumo polypropylene syringes sealed with a cap, found losses of 6% after 60 days when stored refrigerated or frozen.

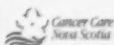
Compatibility:

It is recommended that octreotide not be mixed with other drugs.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status- Basic Level;
Indication restriction- Provincial Cancer Drug Formulary

Community Level: Take Home Prescription
CDHA Formulary Status Formulary- Restricted
Severe chemotherapy-induced diarrhea;
symptoms from carcinoid tumours, or VIPomas
Pharmacare Formulary Status



ONDANSETRON

(Antiemetic; Serotonin [5-HT₃]-Antagonist)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Zofran® Vials with 40mg/20mL, 8mg/4mL

Tablets with 4mg, 8mg; ODT Tablets with 4mg, 8mg

MECHANISM OF ACTION

Selective serotonin receptor (5-HT₃) antagonist, blocking serotonin both peripherally (primary site of action) and centrally in the chemoreceptor trigger zone.

PHARMACOKINETICS

Oral Absorption

well absorbed; bioavailability: 56% to 71%

Distribution

Excretion in breast-milk unknown
cross blood brain barrier? Yes
Vd- 2.2-2.5 L/kg PPB- 70% to 76%

Metabolism

extensively metabolized in liver;
hydroxylation, then glucuronide and/or
sulfate conjugation. Some
demethylation also occurs

Excretion

44% to 60% of a dose is excreted
recovered in the urine, primarily as
metabolites (5% to 10% as unchanged
drug); ~25% appears in the feces.

Urine 44% to 60%, 5% to 10%
unchanged

t_{1/2} - Elimination: 3-5.5 hours.

Adults: 4 hours

Children <15 years: 2-3 hours

SIGNIFICANT INTERACTIONS

cross-sensitivity to granisetron or
dolasetron
mild cytochrome P-450 enzyme
substrate, cytochrome P-450 2D6 and
3A enzyme substrate (eg,
barbiturates, carbamazepine, rifampin,
phenytoin, phenylbutazone, cimetidine,
allopurinol, disulfiram).

CLINICAL MONITORING

NO RECOMMENDED TOXICITY
RATINGS

CONTRAINDICATIONS

- hepatic function impairment
- abdominal surgery
- sensitivity to ondansetron,
granisetron, or dolasetron

IV COMPATIBILITY

Normal Saline, 5% Dextrose

ROUTES

orally

I.V., as a short (15 to 30 min) or
continuous 24 hours infusion

ADMINISTRATION

- Mix in 50-100mL minibag (5%
Dextrose, Normal Saline); Give over
15-30 minutes
- May be admixed with Dexamethasone
in same minibag
- Pre-chemotherapy and pre-radiation
doses should be given 30-45 minutes
prior to chemotherapy or radiation
therapy

EXTRAVASATION HAZARD

no

INDICATIONS AND OTHER USES

Prevention of nausea & vomiting from
emetogenic chemotherapy or radiotherapy

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Injection-Basic Level; *Indication
restriction-* Provincial Cancer Drug
Formulary;

Oral- Take Home Prescription
CDHA Status Formulary- Restricted
Receiving highly emetogenic
chemotherapy or other antineoplastics
not controlled on conventional
antiemetic therapy; receiving
radiotherapy to liver, abdomen or total
body; intolerant/contraindicated to
conventional antiemetic therapy
Pharmacare Status Formulary

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ONDANSETRON

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days) **EARLY ONSET** (days to weeks)
drowsiness, **headache** (24% to 40%), constipation, sedation, diarrhea
fever
flushing, blurred vision

DOSING

Standard dosing:

- 8mg PO or IV (infuse IV over 15 minutes), starting 30-45 minutes before chemotherapy. 8mg PO (or IV for inpatients) q12h for 3 doses after last dose of chemotherapy
- For multiple-day chemotherapy, give ondansetron before each daily dose of chemotherapy and 12 hours later
- For radiotherapy, 4 mg - 8 mg 30-45 minutes prior to radiotherapy followed by 4-8 mg every 12 hours post radiotherapy for 2-5 days
- Ondansetron should be administered with dexamethasone for superior effectiveness
- May use ODT tablets for more rapid absorption prior to chemotherapy or radiotherapy* Some oncologists prefer to give 8mg po prechemo and 8 mg po q8h after chemo, but there is no conclusive evidence of superiority over q12h dosing

Antiemetic failures:

Other dosing may be indicated in specific regimens

- For *highly emetogenic chemotherapy* which has not been controlled with standard therapy, may follow prechemo dose with 1mg/hr continuous infusion of ondansetron for up to 24 hours, or may give 32mg ondansetron in 50-100mL diluent over 15 minutes or longer prior to chemotherapy as a single dose.

See 'Guidelines For The Management Of Nausea & Vomiting in Cancer Patients' for further dosing details

Pediatric:

Adult intravenous dosing for children 4-18 years

Children 4-11 years- 4mg PO tid 30 minutes pre-chemotherapy, then 4 & 8 hours after chemotherapy. Subsequent 1-2 days, 4mg PO q8h (May use oral solution 4mg/5mL for each dose)

PHARMACEUTICAL CONSIDERATIONS

Tablets: 4mg and 8mg oval-shaped yellow tablets. 4mg and 8mg round white orally disintegrating tablets (ODT).

Oral Solution: 4mg/5mL oral solution- strawberry flavour. Bottles of 50mL.

Injection: Ampoules of 4mg/2mL and 8mg/4mL, preservative-free solution. Vials with 40mg/5mL clear solution with preservative.

Diluted solution for infusion

May be diluted in 50-100mL of suitable diluent (e.g. NS or D5W) and given over 15 minutes or longer prior to chemotherapy

May give as IV push over 2-5 minutes.

Compatibility:

Compatible with D5W, NS, Mannitol 10%, Ringer's solution (including solutions with KCl). May be admixed with dexamethasone (up to 20mg) in 50mL D5W, stable for 2 days on storage at room temperature or 7 days on storage under refrigeration. Y-site compatibility is known for cisplatin, 5-fluorouracil, carboplatin, ceftazidime, cyclophosphamide, doxorubicin, epirubicin, and etoposide.

OXALIPLATIN

(Antineoplastic Agent; Alkylating Agent)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Eloxatin Not Available in Canada

Available on a case-by-case basis through Special Access Program, Health Canada
(call 613-941-2103 /e-mail EDR_Drugs-BPA@hc-sc.gc.ca)

MECHANISM OF ACTION

Alkylating agent. Following intracellular hydrolysis of the "leaving group", the platinum compound binds to DNA, RNA, or proteins. Oxaliplatin is thought to be noncross-resistant with cisplatin and carboplatin, on the basis of lack of recognition of oxaliplatin/DNA adducts by DNA repair systems.

PHARMACOKINETICS

Oral Absorption

No information

Distribution

widely distributed; after a 2-hour infusion:
40% of blood platinum in erythrocytes,
33% bound to plasma proteins, 27%
free in plasma

cross blood brain barrier? No information

Vd- 330-241 L PPB- 99%

Metabolism

extensive biotransformation, up to 11%
components are present in plasma
ultrafiltrate

Active metabolite:

diaminocyclohexane (DACH) platinum
species

Inactive metabolites: several conjugates,
including 1,2-DACH-platinum dichloride
(neurotoxicity)

Excretion

Renal excretion & tissue distribution for
platinum; mainly renal excretion for
platinum metabolites

renal; after 5 days: 54% in urine, <3% in
feces

Urine: 30-50% in 2-5 days

t_{1/2} - erythrocytic platinum: γ-12-50 days;

ultrafilterable platinum: α - 10-25 min

β- 26 hours

Cl- 17.6-9.95 L/h

IV COMPATIBILITY

5% dextrose

water for injection

ROUTES

short I.V. infusion (2-6 hours)
or chronomodulating fashion over multiple
days

ADMINISTRATION

- Mix in 500mL bag (5% Dextrose);
Infuse over 2 hours (increase to 6
hours for toxicity)
- Do **NOT** admix with Normal Saline or
infuse through a Y-site connected to
any solution containing Normal Saline
or any other chlorides

EXTRAVASATION HAZARD

minimal or no

ANTIEMETIC RISK

HIGH RISK (30-90% of patients)

- Use a serotonin receptor antagonist
PLUS dexamethasone pre-
chemotherapy and post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

SIGNIFICANT INTERACTIONS

Normal saline or any other chloride ions
(inactivates oxaliplatin)

Alkaline drugs or solutions (e.g.
Fluorouracil)

Aluminium in needles or I.V. sets
(precipitates oxaliplatin)

Irinotecan (oxaliplatin induces cholinergic
syndrome- prophylactic atropine before
irinotecan if given with oxaliplatin)

Continued Next Page...

OXALIPLATIN

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

neurotoxicity

paresthesias of the hands, feet

perioral region (reversible)

Pharyngolaryngodysesthesia

(altered feeling in mouth & throat,

disrupted breathing pattern or swallow-

ing, enhanced cold temperature

sensitivity)

nausea/vomiting

EARLY ONSET (days to weeks)

* myelosuppression (rare)

peripheral sensory neurotoxicity

DELAYED ONSET (weeks to months)

central neurotoxicity (rare)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Monitoring for symptoms of Pharyngolaryngodysesthesia at each visit, toxicity ratings to track experience

PHARYNGOLARYNGODYSESTHESIA

0. No change

1. Paraesthesia/dysesthesias (P/D) of short duration that resolve and do not interfere with function (may be cold-induced)
2. P/D interfering with function but not activities of daily living (ADL)
3. P/D with pain or functional impairment that also interfere with ADL
4. Persistent P/D that are disabling or life-threatening

Rated At Each Clinic Visit

SUGGESTED CRITERIA

- Neurologic (Sensory) ratings at each visit

SENSORY

0. No change

1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss; moderate paraesthesia
3. Sensory loss interferes with function

Rated At Each Clinic Visit

OXALIPLATIN

DOSING

Intravenous:

1 week:

- 35 mg/m² IV for one dose on day 1

2 weeks:

- 85 mg/m² (range 80-100 mg/m²) IV for one dose on day 1

3 weeks:

- 130 mg/m² (range 85-135 mg/m²) IV for one dose on day 1
- 30 mg/m²/day by continuous IV infusion for 5 consecutive days (total dose per cycle 150 mg/m²)
- 35 mg/m²/day by chronomodulated IV infusion for 5 consecutive days (total dose per cycle 175 mg/m²)

4 weeks:

- 85 mg/m² IV for one dose on days 1 and 15 (total dose per cycle 170 mg/m²)

50 days:

- 50 mg/m² IV for one dose on days 1, 8, 15, 22, 29, 36 (total dose per cycle 300 mg/m²)

Concurrent radiation:

- investigational, 130 mg/m² IV on days 1 and 29 concurrent with radiation

Other dosing may be indicated

NOTES

- Peripheral sensory neurotoxicity is dose-related, cumulative and will usually be reversible within a few months after treatment if stopped. Gabapentin 100mg PO BID, with increasing increments as needed may be effective in management of this toxicity.
- Pharyngolaryngeal dysesthesia may require the infusion time to be increased up to 6 hours; avoid the use of ice chips for stomatitis prevention during oxaliplatin infusion days

GUIDELINES

Visit the **Cancer Care Nova Scotia** website (www.cancercare.ns.ca) for the position paper on Oxaliplatin for colorectal cancer

INDICATIONS AND OTHER USES

OTHER ONCOLOGY USES

*Colorectal cancer
Breast cancer
Gastric cancer
Germ cell cancer
Head and neck cancer
Lung cancer, non-small cell
Lymphoma, non-Hodgkin's
Mesothelioma
Ovarian cancer
Pancreatic cancer
Prostate cancer*

CONTRAINDICATIONS

- association with alkaline drugs or solutions or chlorides including sodium chloride

DOSE ADJUSTMENT CRITERIA

Neurotoxicity: (Suggested action)

- If troublesome but no functional impairment for >7 days (or until next cycle), **REDUCE** dose from 130mg/m² to 100mg/m² or from 85mg/m² to 65mg/m², or from 65mg/m² to 50mg/m²
- If functional impairment for >7 days, **REDUCE** dose from 85mg/m² to 50mg/m²
- If functional impairment persists to next cycle, **DISCONTINUE** Oxaliplatin (may resume therapy if neurotoxicity improves or resolves)

EMERGING INFORMATION

This drug is under investigation and has not been widely used in oncology practice. As new information is discovered, portions of this monograph may become outdated. Refer to primary literature and revisions to official product monograph to ensure that information on this drug is current.

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OXALIPLATIN

PHARMACEUTICAL CONSIDERATIONS

Injection:

50 mg and 100 mg vials.

Reconstitute powder with SWI or D5W to a final concentration of 5 mg/mL (ie, 10 mL diluent for 50 mg vial or 20 mL diluent for 100 mg vial). Never reconstitute powder with NS as oxaliplatin degrades when mixed with chloride containing solution.

Reconstituted solution for injection:

Physically and chemically stable for 48 hours under refrigeration or at room temperature. The manufacturer recommends the solution be stored under refrigeration and used within 24 hours.

Diluted solution for infusion: Dilute in 250-500 mL D5W. Manufacturer recommends oxaliplatin be administered immediately after dilution. Never dilute oxaliplatin in NS as oxaliplatin degrades when mixed with chloride containing solution. Stable for 6 hours at room temperature and for 24 hours under refrigeration.

Compatibility:

Oxaliplatin can be co-administered with leucovorin infusion using a Y-line placed immediately before the site of injection. However, the drugs should not be combined in the same infusion bag. Leucovorin must be diluted using isotonic infusion solutions such as D5W but not NS or alkaline solutions.

Incompatibility:

The following are incompatible via Y-site injection or in the same infusion solution: alkaline drugs or solutions (eg, fluorouracil, leucovorin), chlorides (including sodium chloride at all concentrations). Aluminum-containing IV needles, syringes or sets should not be used to prepare or administer oxaliplatin; aluminum reacts with platinum from oxaliplatin to form a precipitate, resulting in loss of potency.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-

Intermediate Level- not

commercially available in Canada

CDHA Status

Non-Formulary

Pharmacare Status

Non-Formulary

PACLITAXEL

(Antineoplastic Agent; Antimicrotubular)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Taxol® Vials with 30mg/5mL, 100mg/16.7mL, 300mg/50mL

Protect from light

MECHANISM OF ACTION

Causes formation of stable microtubule bundles by promoting assembly and preventing depolymerization, interfering with the late G2 mitotic phase, and inhibiting cell replication; it may also suppress cell proliferation and modulate immune response.

PHARMACOKINETICS

Oral Absorption

not absorbed orally

Distribution

Vd indicates extensive extravascular distribution and/or tissue binding;

enters breast-milk

cross blood brain barrier? No

Vd 334 L/m² 42-162 L/m²; children:

PPB 95% to 98%

Metabolism

uncertain, hepatic metabolism and biliary secretion probably account for the majority of elimination

metabolite(s): active, inactive- no information

Excretion

primarily as unchanged drug and unidentified metabolites in bile

Urine: 5-6 % as unchanged drug

Cl 100-993 mL/min/m²; children: 123-161 mL/min/m²

EXTRAVASATION HAZARD

IRRITANT (cellulitis, inflammation)

Management- stop IV, aspirate, elevate limb, warm intermittent compresses

Follow Extravasation Guidelines

SIGNIFICANT INTERACTIONS

amifostine, anticonvulsants, bone marrow depressant agents, CNS depressants, doxorubicin, drugs affecting hepatic microsomal enzymes, epirubicin, phenytoin, quinidine, radiation therapy, vinorelbine, vitamin A

Cytochrome P450 Substrate

IV COMPATIBILITY

normal saline, dextrose 5%, lactated

Ringer's

incompatible with PVC administration sets, containers or equipment

ROUTES

intermittent IV (1.2 mg/mL over 3 hours)

continuous IV (1.2 mg/mL over 24 hours)

ADMINISTRATION

Always use non-PVC tubing with a 0.22 micron in-line filter

- Mix in 500-1000mL polyolefin bag or glass bottle (Normal Saline or 5% Dextrose- dilution concentration 0.3-1.2 mg/mL); Use non-PVC equipment (polyethylene-lined nitroglycerin tubing sets), including 0.22 micron in-line filter. Infuse over 3 hours
- Take a baseline blood pressure measurement, if prior hypotension noted
- May be infused over 1 hour- mix in 250mL bag as above
- May be given as 24 hour infusion- mix in 1000mL bag and use non-PVC equipment and in-line filter; given as inpatient or using ambulatory infusion pump
- ALWAYS premedicate with Dexamethasone (20mg PO 12 & 6 hrs preChemo), Diphenhydramine 50mg IV & Ranitidine 50mg IV 30-60 minutes preChemo

Continued Next Page...

PACLITAXEL

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

- * anaphylaxis (2%) and **allergic reactions** (41%) (pretreatment, monitoring and on-hand emergency medications required)
- nausea and vomiting** (59%, usually mild to moderate, severe 7%)
- diarrhea** (43%)
- decreased heart rate during infusion (10%, bradycardia)
- low blood pressure during infusion (23%, hypotension)
- vein irritation (phlebitis, erythema, tenderness, discomfort)
- radiation recall reaction (rare)

EARLY ONSET (days to weeks)

- * **low WBC, RBC, platelets** (**myelosuppression**, nadir 8-11 days, recovery 15-21 days)
- hair loss (alopecia)** 82%, usually total
- nerve problems** (62%, peripheral neuropathy, 4% severe)
- muscle and joint pain** (55%, myalgia, arthralgia, usually mild, onset 2-8 days, duration 4-7 days)
- mouth sores** (39%, mucositis, dose-related, severe 1%)
- * **heart problems** (19-30%, ECG changes, severe 2%)
- liver problems (elevated liver function tests)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- Watch for symptoms of **fever or infection**
- Neurologic (Sensory), hypersensitivity and flu-like symptoms toxicity ratings at each visit
- Baseline **blood pressure and pulse rate monitoring**

HYPERSENSITIVITY

- 0 None
1. Transient rash, fever $<38^{\circ}\text{C}$
2. Urticaria, fever $\geq 38^{\circ}\text{C}$, mild bronchospasm
3. Serum sickness, bronchospasm, requires parenteral medications
4. Anaphylaxis
(Arthralgia, myalgia)

SUGGESTED CRITERIA

- Baseline **liver function tests** (if liver failure suspected) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- Periodic **renal function tests** [serum creatinine, electrolytes & BUN]
- **Blood pressure and pulse rate monitoring** during drug administration (& for the following hour)

FLU-LIKE SYMPTOMS

0. None
 1. Mild
 2. Moderate
 3. Severe
- SENSORY**
- 0 No change
 - 1 Mild paraesthesia, no deep tendon reflex
 - 2 Mild/moderate sensory loss, moderate paraesthesia
 - 3 Sensory loss interferes with function
- Rated At Each Clinic Visit**

PACLITAXEL

DOSING

To minimize severe hypersensitivity reactions, patients should be premedicated with:

- dexamethasone 20 mg po 12 and 6 hours before, OR 20 mg IV 30 minutes before,
- diphenhydramine 50 mg IV 30-60 minutes before, and ranitidine 50 mg IV 30-60 minutes before.
- In the event of a treatment delay (eg, admixture is not available) additional doses are required.

Intravenous:

- q3w: 135-250 mg/m² over 3 hours (decreased neutropenia) or 24 hours (decreased hypersensitivity)
- Note: schedules from 1-96 hours are being studied

Pediatric

- Safety & effectiveness not established
Other dosing may be indicated

DOSE ADJUSTMENT CRITERIA

Hepatic dysfunction (*Suggested action*)

Maximum 135mg/m² if AST > 70IU/L or Bili ≤ 25μmol/L;

Maximum 75mg/m² if Bili = 25-50μmol/L;

Maximum 50mg/m² if Bili > 50μmol/L

INDICATIONS AND OTHER USES

- Breast cancer
- Ovarian cancer

OTHER ONCOLOGY USES

Head and neck cancer

Lung cancer

Occult cancers (unknown primary)

CONTRAINDICATIONS

- use with caution in patients with known hypersensitivity to paclitaxel
- use with caution in patients with known hypersensitivity to drugs formulated in Cremophor EL® (eg, teniposide, cyclosporine)
- pregnancy and breast feeding
- some heart problems (2nd or 3rd degree heart block)

ANTIEMETIC RISK

INTERMEDIATE RISK (10-30% of patients)

- Use a dexamethasone pre-chemotherapy and a dopamine receptor antagonist PRN post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

PACLITAXEL

PHARMACEUTICAL CONSIDERATIONS

Injection

6 mg/mL preservative-free solution in polyethoxylated castor oil (Cremophor EL) and dehydrated ethanol. Store at room temperature and protect from light during storage. Refrigeration or freezing do not adversely affect the drug. To prevent leaching of the plasticizer DEHP [di-(2-ethylhexyl)phthalate] from PVC, avoid contact between paclitaxel and PVC equipment or devices during preparation. Use of a plastic syringe to measure a dose is acceptable but drug-syringe contact time should be minimized. Contraindicated in patients with a history of severe hypersensitivity reactions to products containing Cremophor® EL (ie. cyclosporin)

Diluted solution for infusion

Compatible with NS, D5W, D5-NS or dextrose 5% in Ringer's injection at 15 - 30° C for up to 27 hours. Dilutions may appear hazy due to the Cremophor vehicle. Glass, polypropylene or polyolefin storage containers should be used and contact with PVC should be avoided. Paclitaxel should be diluted to a final concentration of 0.3-1.2 mg/mL.

Because small numbers of fibers have been observed in solution (within acceptable limits set by the USP), filtration during administration using a 0.2 or 0.22 micron in-line filter (with short inlet and outlet PVC sections, eg. IVEX-2) is necessary. Non-PVC (eg. polyethylene or polyethylene-lined) administration sets should be used. Compatible during simulated Y-site injection with carboplatin, cimetidine, cisplatin, cyclophosphamide, cytarabine, dexamethasone, diphenhydramine, doxorubicin, etoposide, fluorouracil, haloperidol, lorazepam, methotrexate, metoclopramide, prochlorperazine, ranitidine and vancomycin. Paclitaxel should not be mixed with other drugs.

GUIDELINES

Visit the **Cancer Care Nova Scotia** website (www.cancercare.ns.ca) for the guideline on Paclitaxel for ovarian cancer

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Intermediate Level; *Indication
restriction-* Provincial Cancer Drug
Formulary

CDHA Status Formulary- Restricted
Pharmacare Status Non-Formulary

PAMIDRONATE

(Biphosphonate; Calcium-Lowering Agents)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Aredia®

Vials with 30mg, 60mg, 90mg for reconstitution

Generic products available.

MECHANISM OF ACTION

Pamidronate binds to hydroxyapatite and inhibits osteoclastic bone resorption; unlike etidronate, pamidronate is not associated with inhibition of bone mineralization.

PHARMACOKINETICS

Oral Absorption

very low (1%)- diminishes when given with food or calcium

Distribution

45-53% adsorbed to bone, mostly in areas of high turnover; stomach, liver, spleen, tracheal cartilage, macrophages; excretion in breast-milk unknown cross blood brain barrier? No information Vd, PPB- No information

Metabolism

No metabolism

Excretion

renal; non-renal clearance is a result of uptake by bone, with subsequent slow elimination via bone turnover;

Urine: yes; I.V.: 30% unchanged within 12 hours

$t_{1/2} \alpha$ - 0.6 hours $t_{1/2} \beta$ - in bone, 300 days

Cl- 1.1mL/min

IV COMPATIBILITY

sodium chloride 0.45% or 0.9%
dextrose 5%

ROUTES

intravenous infusion over 2 to 4 hours, or longer
intravenous injection
longer infusion time if renal failure

ADMINISTRATION

- Mix in 250-500mL solution (5% Dextrose, Normal Saline) and infuse over 2 to 4 hours (longer infusion time if Creatinine >180mmol/L or renal impairment)
- May infuse using ambulatory infusion device over 2-5 hours

Hypercalcemia indication

- 30-60mg Dose: Mix in 250-500mL solution (5% Dextrose, Normal Saline) and infuse over 2 hours (longer infusion time if Creatinine >180mmol/L or renal impairment)
- 90mg Dose: Mix in 500-1000mL solution (5% Dextrose, Normal Saline) and infuse over 4 to 6 hours

EXTRAVASATION HAZARD

local thrombophlebitis at infusion site

DOSING

Intravenous:

Multiple myeloma

4-6 weeks:

- 90 mg IV for one dose on day 1

Osteolytic bone metastases

3-4 weeks:

- 90 mg IV for one dose on day 1

Malignancy-related hypercalcemia

- 90 mg (30-90 mg) IV for one dose

Pediatric:

Intravenous:

- 1-2 mg/kg IV over 3-24 h has been used for malignancy-related hypercalcemia

Other dosing may be indicated

INDICATIONS AND OTHER USES

- Malignancy-related hypercalcemia
- Multiple myeloma
- Osteolytic bone metastases

CONTRAINDICATIONS

- cardiac failure (avoid overhydration, use smaller infusion volume)
- renal function impairment

SIGNIFICANT INTERACTIONS

calcium-containing compounds, magnesium-, iron- or aluminum-containing compounds, vitamin D & analogs, calcitonin, foscarnet food- milk products

Continued Next Page...

PAMIDRONATE

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET

nausea- 45%, **vomiting**- 32%
hypocalcemia (usually with higher doses)

EARLY ONSET (days to weeks)

leukopenia
flu-like symptoms (transient fever- 36%, arthralgias- 12%, malaise, headache)
skeletal pain (59%)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Serum electrolytes, including serum calcium levels
HYPOCALCEMIA

0. Serum Calcium >2.10 mmol/L
1. Serum Calcium =2.10 to 1.93 mmol/L
2. Serum Calcium =1.92 to 1.74 mmol/L
3. Serum Calcium =1.73 to 1.51 mmol/L
4. Serum Calcium <1.50 mmol/L

Rated on assessment of anti-hypercalcemia response and at periodic visits or in response to patient complaint

SUGGESTED CRITERIA

- Periodic renal function tests, on repeat doses [serum creatinine, electrolytes & BUN]
 - Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment, especially if fever
- HYPERCALCEMIA- Response Criteria

0. Serum Calcium <2.64 mmol/L
1. Serum Calcium =2.64 to 2.88 mmol/L
2. Serum Calcium =2.89 to 3.12 mmol/L
3. Serum Calcium =3.13 to 3.37 mmol/L
4. Serum Calcium >3.37 mmol/L

Rated on assessment of anti-hypercalcemia response and at periodic visits or in response to patient complaint

PHARMACEUTICAL CONSIDERATIONS

Injection:

30 mg and 90 mg vials; as anhydrous pamidronate disodium; preservative-free 8 Store at room temperature.

Reconstitute each 30 mg and 90 mg vial with 10 mL of SWI to yield pamidronate concentrations of 3 mg/mL and 9 mg/mL, respectively. Reconstituted solution is stable for 24 hours at room temperature.

Diluted solution for infusion:

Must be further diluted with NS or D5W to concentrations less than or equal to 0.36 mg/mL. Diluted solution is stable for 24 hours at room temperature.

Compatibility:

Pamidronate should not be mixed with calcium-containing IV solutions such as Ringer's solution.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Basic Level

CDHA Status Formulary

Pharmacare Status Non-Formulary

PEGFILGRASTIM

(Granulocyte Colony Stimulating Factor (G-CSF))

Revision Date: Jul 04

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Neulasta® Prefilled syringes with 6mg/0.6mL

Keep under refrigeration

MECHANISM OF ACTION

Pegfilgrastim is a covalent conjugate of recombinant methionyl human G-CSF (Filgrastim) and monomethoxypolyethylene glycol. Pegfilgrastim stimulates the production, maturation, and activation of neutrophils and activates neutrophils to increase both their migration and cytotoxicity.

PHARMACOKINETICS

Oral Absorption

inactive orally

Distribution

non-linear pharmacokinetic profile
excretion in breast-milk unknown
cross blood brain barrier? No information
Vd, PPB- No information

Metabolism

systemic

metabolite(s):

active, inactive- No information

Excretion

clearance from serum directly related to
number of neutrophils- as neutrophils
recover from neutropenia, serum
clearance increases- individual variation!
t_{1/2} 15-80 hours
Cl variable- decreased when dose
increased

ROUTES

subcutaneous

EXTRAVASATION HAZARD

none

INDICATIONS AND OTHER USES

- Prevent neutropenia which interferes with potentially curative chemotherapy
- OTHER ONCOLOGY USES**
Rescue of febrile neutropenic patients
Stimulate engraftment post BMT

CONTRAINDICATIONS

- Patients with known hypersensitivity to *E coli*-derived proteins, pegfilgrastim, Filgrastim, or any other component of the product.
- Do not administer within 14 days before and 24 hours after administration of cytotoxic chemotherapy

DOSING

- single dose of 6mg SC for each chemotherapy cycle, at least 24 hours after chemotherapy

SIGNIFICANT INTERACTIONS

No formal drug interaction studies between Pegfilgrastim and other drugs have been performed.
Lithium- may potentiate the release of neutrophils

PEGFILGRASTIM

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)

- * splenic rupture- left upper abdominal/shoulder tip pain (rare)
dull pain in long bones, back, pelvis
(first 2-3 days of treatment)
arthralgia, myalgia, headache

EARLY ONSET (days to weeks)

- * adult respiratory distress syndrome (ARDS)- (rare)
skin rash (Sweet's syndrome & other dermatoses)
increased serum uric acid, LDH, alkaline phosphatase

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Monitor consecutive **complete blood count including differential, hematocrit & platelet count (CBC)** results before chemotherapy and at least 1-2 times weekly

SUGGESTED CRITERIA

- Periodic **clinical assessment of cardiac function** (if pre-existing cardiac condition)

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level for Take Home
prescription

CDHA Status Non-Formulary

Pharmacare Status Non-Formulary

PEMETREXED

(Antineoplastic Agent)

Revision Date: Jul 04

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Alimta®

Other Name: LY231514

MECHANISM OF ACTION

Pemetrexed is an antifolate agent that inhibits thymidylate synthase (TS), dihydrofolate reductase (DHFR), and glycinamide ribonucleotide formyltransferase (GARFT), thus blocking purine synthesis. Pemetrexed is transported into cells by the membrane folate binding protein transport systems and the reduced folate carrier. In the cell, pemetrexed is polyglutamated by folyl polyglutamate synthase. It is the polyglutamate forms which are potent inhibitors of TS and GARFT. Polyglutamation is time- and concentration-dependant in tumour cells and, to a lesser extent, normal cells. Polyglutamated metabolites have an increased intracellular half-life and a prolonged drug action in malignant cells.

PHARMACOKINETICS

Oral Absorption

no information

Distribution

AUC does not change over multiple cycles, but increases if renal function impaired

Vd- 16 L PPB- 81%

Metabolism

minimal metabolism

metabolite(s): no information

Excretion

primarily renal excretion- 70-90% total dose as unchanged drug in urine in first 24 hours

Elimination t_{1/2} = 3.5 hours (normal renal function)

Cl- 91.8 mL/min; increased in patients with renal dysfunction

ROUTES

intravenous infusion over 10 minutes

ADMINISTRATION

- Mix in 100 mL minibag (Normal Saline). Infuse over 10 minutes.
- Pretreatment with dexamethasone 4 mg PO BID for 3 days (on the day before, the day of and the day after treatment)
- Pretreatment with folic acid 400 mcg daily for at least 5 of 7 days preceding pemetrexed treatment (may use a multivitamin preparation which includes 5 mg folic acid), and vitamin B₁₂ 1000 mcg IM injection one week before first dose of pemetrexed and every 3 cycles thereafter

ANTIEMETIC RISK

HIGH RISK (in Combination with Cisplatin)

- See Cisplatin monograph for antiemetic therapy
- No additional antiemetics needed for pemetrexed treatment

IV COMPATIBILITY

sodium chloride 0.9% (preservative-free)

NOT compatible with calcium-containing diluents

EXTRAVASATION HAZARD

not a vesicant

SIGNIFICANT INTERACTIONS

NSAIDs reduce pemetrexed clearance
Oral folic acid and IM vitamin B₁₂ do not affect pharmacokinetics of pemetrexed

CONTRAINDICATIONS

- Hypersensitivity to pemetrexed or any other ingredients in product

Continued Next Page...

PEMETREXED

SIDE EFFECTS

* may be life-threatening

side effects in **bold**, *italic* type are common

Side effects which are slightly increased when pemetrexed added to cisplatin

IMMEDIATE ONSET (hours to days)

diarrhea (26%)

nausea (84%), *vomiting* (58%)

Side effects (especially myelosuppression and nausea & vomiting) are increased when patients do not receive supplementation with folic acid and vitamin B₁₂

EARLY ONSET (days to weeks)

* **myelosuppression** (58% neutropenia, 33% anemia, 27% thrombocytopenia)
* **fever** (17%), **infection** (11%)
stomatitis/pharyngitis (28%)
skin rash/desquamation (22%)
fatigue (80%), constipation (44%), anorexia (35%)

CLINICAL MONITORING

RECOMMENDED CRITERIA (in addition to clinical monitoring for Cisplatin)

- Clinical assessment of **stomatitis**, oral examination upon patient complaint of a sore mouth

STOMATITIS (Pharyngitis)

- 0 None
- 1 Painless ulcers, erythema, or mild soreness in the absence of lesions
- 2 Painful erythema, edema, or ulcers, but can eat or swallow
- 3 Painful erythema, edema, or ulcers requiring IV hydration
- 4 Severe ulceration or requires parenteral or enteral nutritional support or prophylactic intubation

Rated at each visit

DOSING

Intravenous

3 week

- 500 mg/m² IV for one dose on day 1, followed 30 minutes later by cisplatin 75 mg/m² IV

Pediatric

- Safety & effectiveness not established

INDICATIONS AND OTHER USES

- In combination with cisplatin for the treatment of patients with malignant pleural mesothelioma which is unresectable or not a surgical candidate

DOSE ADJUSTMENT CRITERIA

Renal Failure, (*Suggested action*)

- If Cr Cl < 45 mL/min. **OMIT** pemetrexed dose

Hematologic Toxicities, (*Suggested action*)

- If ANC < 0.5 x 10³/L and platelets > 50 x 10³/L, **reduce to 75% dose**
- If platelets > 50 x 10³/L, **reduce to 50% dose**

Non-Hematologic Toxicities, (*Suggested action*)

- If Grade 3 or 4 toxicity, **reduce to 75% dose**
- If diarrhea which requires hospitalization, **reduce to 75% dose**
- If Grade 3 or 4 stomatitis, **reduce to 50% dose**

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PEMETREXED**PHARMACEUTICAL CONSIDERATIONS**Injection:

500 mg vial of lyophilized powder for reconstitution. Contains 500 mg mannitol and pH buffers. Store at room temperature.

Reconstitute powder with 4 mL SWI to a final concentration of 0.5 mg/mL.

Reconstituted solution for injection:

Reconstitute with 20 mL of 0.9% sodium chloride solution (preservative-free) to a concentration of 25 mg/mL. Solution should be clear to light yellow/green and particulate-free. Further dilution is required.

Chemically and physically stable for up to 24 hours at room temperature or refrigeration, when exposed to ambient light; however, it is recommended that pemetrexed be refrigerated to avoid bacterial contamination.

Diluted solution for infusion:

Dilute in 100 mL NS. Chemically stable for 24 hours at room temperature exposed to ambient light. If not used promptly, it is recommended that pemetrexed be refrigerated to avoid bacterial contamination.

Compatibility: It is not recommended that pemetrexed may be mixed with other drugs.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Intermediate Level; indication
restrictions

CDHA Status	Non-Formulary
Pharmacare Status	Non-Formulary

PREDNISONE

(Adrenal Corticosteroid, Anti-inflammatory Agent, Glucocorticoid)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name Deltasone®

Tablets with 5mg, 50mg Prednisone

Generic products available

MECHANISM OF ACTION

Antitumor effects may be related to inhibition of glucose transport, phosphorylation, or induction of apoptosis in immature lymphocytes. Antiemetic effects are thought to occur due to blockage of innervation of the emetic center via inhibition of prostaglandin synthesis.

PHARMACOKINETICS

Oral Absorption

rapidly and almost completely

Distribution

muscles, liver, skin, intestines, kidneys,
enters breast-milk

cross blood brain barrier? No information
(crosses placenta)

Vd- 0.4-1 L/kg PPB- yes 65% to 91%
(concentration dependent)

Metabolism

primarily hepatic (rapid), renal and tissue;
ketone group at C-11 must be reduced;
rapidly converted to prednisolone

metabolite(s): active- prednisolone
inactive- yes, most metabolites

Excretion

primarily by renal excretion of inactive
metabolites (glucuronides, sulfates,
and unconjugated)

Urine: small amount of unmetabolized
drug

t½ - 2.5-3.5 hours. Prednisolone:
biologic: 18-36 hours, End-stage renal
disease: 3-5 hours

ROUTES

oral

INDICATIONS AND OTHER USES

- Leukemias & lymphomas, palliative management
- Multiple non-oncology indications

CONTRAINDICATIONS

- arthroplasty of joints
- thromboembolic disorders
- osteoporosis (juxta-articular, non-arthritic)

SIGNIFICANT INTERACTIONS

NSAIDs, ASA, potassium-depleting agents (eg loop diuretics), asparaginase, barbiturates, phenytoin, ketoconazole, estrogens

Cytochrome P450 Substrate

DOSING

Oral

- 5-60 mg po in single or divided doses (1-4 times daily, as specified in regimen)
- Many other doses and combinations used in oncology
- Take tablets with food; if possible, do not take at bedtime (qhs specified in some regimens)

Other dosing may be indicated

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PREDNISONE

SIDE EFFECTS

* may be life-threatening

side effects in ***bold, italic*** type are common

IMMEDIATE ONSET (hours to days)

weight gain, increased appetite
hyperglycemia
insomnia

EARLY ONSET (days to weeks)

* ***immunosuppression***
acniform skin rash
proximal myopathy
mood swings
hypertension

DELAYED/LATE ONSET

Cushing's syndrome
osteoporosis

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Serum glucose levels** (monitor routinely for diabetic patients)

SUGGESTED CRITERIA

- **Serum glucose levels** (monitor periodically for all other patients) and **serum electrolyte levels**

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level Take Home
Prescription

CDHA Status	Formulary
Pharmacare Status	Formulary

PROCARBAZINE

(Antineoplastic Agent; Alkylating Agent)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Mutulan® White capsules with 50mg

MECHANISM OF ACTION

Procarbazine is a nonclassic alkylating agent. It is activated intracellularly to compound(s) that bind covalently to DNA.

PHARMACOKINETICS

Oral Absorption

rapid and complete

Distribution

highest levels in liver, kidney, intestinal wall and skin

cross blood brain barrier? yes, rapid equilibration

Vd. PPB- no information

Metabolism

liver metabolism by microsomal enzyme oxidation system

metabolite(s): active- yes

inactive- yes (N-isopropyl-terphthalamic acid)

Excretion

renal (70% within 24 hours as metabolites), 30% as metabolites through the respiratory tract, predominantly in urine as N-isopropyl-terphthalamic acid

Urine. 70% within 24 hours (metabolite)

t_{1/2} α - 7 minutes (parent compound)

t_{1/2} β - 1 hour

ROUTES

oral

DOSING

Round dose to the nearest 50 mg.

Oral:

- q3w: 100 mg/m²/day po x 2 days
- q4w: 100 mg/m²/day po x 7-14 days
- q6w: 60 mg/m²/day po x 14 days
- Total daily dose may be taken at a single time or in divided fractions throughout the day. The latter regimen may cause less acute toxicity

Pediatric

- q4w: 100 mg/m²/dose po x 7-14 days
- q2-4w: 75 mg/m²/dose po

Other dosing may be indicated

INDICATIONS AND OTHER USES

- Hodgkin's disease
- Non-Hodgkin's lymphoma

OTHER ONCOLOGY USES

Brain tumours

SIDE EFFECTS

* may be life-threatening

IMMEDIATE ONSET (hours to days)

- * anaphylaxis (rare)
- allergic (rare, serum sickness, fever)
- nausea and vomiting** (>50%)
- flu-like syndrome
- radiation recall reaction (rare)

DELAYED/LATE ONSET (weeks- years)

- lung problems (acute infiltrate, edema, cough)
- eye problems (rare, double vision)
- CNS depression and other effects (10-30%)
- * cancer (leukemia)
- nerve damage (10-20%, peripheral)

side effects in **bold, italic** type are common

EARLY ONSET (days to weeks)

- * **low WBC, RBC, platelets**
- (myelosuppression)**, nadir 14-21 days, recovery 28 days)
- lung problems (acute infiltrate, edema, cough)
- eye problems (rare, double vision)
- mouth sores (stomatitis)
- hair loss (rare, alopecia)
- appetite loss (anorexia)
- skin problems (rash, urticaria, hyperpigmentation)
- blood problems (hemolytic anemia)
- infertility (amenorrhea, azoospermia)
- CNS depression and other effects (10-30%)

PROCARBAZINE

SIGNIFICANT INTERACTIONS

alcohol, allopurinol, anticonvulsant drugs, antidepressants, antidiabetics, buspirone, carbamazepine, CNS depressants, dextromethorphan, digoxin, dobutamine, food, morphine, selective serotonin reuptake inhibitors, sumatriptan, sympathomimetic agents, tricyclic antidepressants, tyramine-rich foods, other antineoplastic agents

NOTE

PROCARBAZINE - DIET INFORMATION

- The foods listed below may interact with PROCARBAZINE and cause severe reactions, such as headache, heart palpitations, high blood pressure, nausea, vomiting, and diarrhea. These reactions are caused by the alcohol and/or tyramine content of the food or drink.
- The diet changes recommended below should be followed during the days when taking PROCARBAZINE, and also for 10-14 days after the medication is finished.

Food Groups	Allowed	Avoid	Limit to 1/2 cup, 4 oz or 125 mL/day
Milk & Milk Products	All milk drinks, cream cheese, cottage cheese. All milk and milk products to be used well within "BEST BEFORE" date.	All other cheeses, especially aged cheese, foods containing aged cheese; processed cheese.	Chocolate milk, yogurt.
Breads & Cereals	All		
Meat & Alternatives	All except those to avoid. Meat, fish and poultry should be freshly prepared. Refrigerated storage should be brief.	Smoked or pickled fish (eg. pickled herring); aged and fermenting meats, fish, poultry, and game; corned beef, liver, liver pâté, dry fermented sausage (eg. salami, pepperoni, summer sausage, bolognas)	
Fruits & Vegetables	All except those to avoid.	Broad beanpods (eg. lima, fava beans); banana peel, sauerkraut, overly ripe fruits and vegetables.	*Raisins, ripe avocado, raspberries
Fats & Oils	All		
Miscellaneous	Baker's yeast	Yeast vitamin supplements (eg. Brewer's yeast), Yeast and meat extracts (eg. Oxo®, Bovril®, consommé, chicken broth, Marmite®), Tofu, all alcoholic beverages, including beer and wine.	Dried soup and gravy bases; *chocolate, caffeine, *soy sauce.

* Small quantities are recommended

PROCARBAZINE

DRUG

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Periodic clinical pulmonary exam** including auscultation, pulmonary toxicity ratings (Cough, SOB)

SUGGESTED CRITERIA

- Routine **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- Periodic **renal function tests** [serum creatinine, electrolytes & BUN]

SHORT OF BREATH

- 0 No change
- 1 Abnormal Pulmonary Function Tests
- 2 Dyspnea on exertion
- 3 Dyspnea at normal level of activity
- 4 Dyspnea at rest

COUGH

- 0 None
- 1 Mild
- 2 Moderate
- 3 Severe

Rated At Each Clinic Visit Every 2-3 Months

CONTRAINDICATIONS

- known hypersensitivity to procarbazine
- pregnancy and breast feeding
- low WBC, RBC, platelets (myelosuppression)

ANTIEMETIC RISK

HIGH RISK (30-90% of patients)

- Use a serotonin receptor antagonist PLUS dexamethasone pre-chemotherapy and post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

PHARMACEUTICAL CONSIDERATIONS

Capsules

50 mg; store at room temperature (15-30°C) in tightly-closed, light-resistant containers. Gluten-, lactose-, sodium-, sulfite- and tartrazine-free. Contain mannitol, cornstarch, gelatin, talc, potassium sorbate, methyl- and propylparaben, titanium dioxide and dyes.

DOSE ADJUSTMENT CRITERIA

Renal failure: (Suggested action)
Consider dose reduction if renal function is reduced (eg. reduced creatinine clearance/serum creatinine)

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level: Take home
prescription on preprinted Physician
Standing Order

CDHA Status Formulary
Pharmacare Status Formulary

NOTE: It is recommended to limit
ordering of this medication to preprinted
Physician Standing Order form, for
patient safety

PROCHLORPERAZINE

(Antiemetic/Antivertigo/Antipsychotic Agent)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Stemetil® Peach-coloured tablets with 5mg, 10mg
Generic products available Suppositories with 10mg. Oral liquid with 5mg/5mL
Ampuls with 10mg/2mL

MECHANISM OF ACTION

Prochlorperazine acts on the central and autonomic nervous system; it has weak anticholinergic effects, moderate sedative effects, and strong extrapyramidal effects. Prochlorperazine has strong antiemetic activity. The precise mechanism of antiemetic action is unclear but the drug inhibits apomorphine-induced vomiting and has been shown to directly affect the medullary chemoreceptor trigger zone (CTZ), apparently by blocking dopamine receptors in the CTZ.

PHARMACOKINETICS

Oral Absorption

generally well absorbed, may be erratic

Distribution

Prochlorperazine and metabolites: into most body tissues and fluids, with high concentration being distributed into the brain, lungs, liver, kidneys, spleen; crosses the placenta. Excretion in breast-milk unknown.

cross blood brain barrier? Yes

Vd- no information PPB- high

Metabolism

Exact metabolic fate has not been clearly established. Extensively metabolized, principally in the liver via hydroxylation, oxidation, and conjugation with glucuronic acid; metabolic alterations in the side chain may also occur. Most metabolites: pharmacologically inactive

Excretion

In urine and feces, biliary elimination, principally as metabolites; also appears to undergo enterohepatic circulation

Urine: yes

t½, Cl- no information

IV COMPATIBILITY

Normal saline, 5% Dextrose, Ringer's solution

ROUTES

orally

rectally

I.M.

I.V. injection

I.V. infusion

ADMINISTRATION

- Slow push through sidearm of free flowing IV (5% Dextrose, Normal Saline) over 2 or more minutes (maximum rate = 5mg/minute); patient should remain in supine position during and following administration; monitor blood pressure every 15 minutes during and for 30 minutes post infusion (administering nurse should be certified to administer IV push chemotherapy agents)
- May mix dose in 100mg minibag (Normal Saline); Infuse over 30 minutes

EXTRAVASATION HAZARD

yes, local irritation

CONTRAINDICATIONS

- Management of nausea and vomiting associated with chemotherapy or radiotherapy

- children or adolescents with suspected Reye's syndrome
- in children during surgery or in conditions for which pediatric dosage has not been established

Continued Next Page...

PROCHLORPERAZINE

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)	EARLY ONSET (days to weeks)
<i>sedation, drowsiness</i>	<i>extrapyramidal reactions, dizziness</i>
<i>hypotension</i>	hepatotoxicity
tachycardia (especially with rapid intravenous administration)	photosensitivity
contact dermatitis	CNS depression, respiratory and/or vasomotor collapse.
	seizures

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Observe for signs of **tardive dyskinesia** and other movement disorders

INVOLUNTARY MOVEMENT

- None
- Mild agitation, restlessness
- Moderate agitation
- Torticollis, oculogyric crisis, severe agitation

Rated at each clinic visit or in response to patient complaint

SUGGESTED CRITERIA

- Periodic **blood pressure measurement**
- Baseline & periodic **hepatic function tests** (if impairment suspected) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]
- Baseline & periodic **renal function tests** (if impairment suspected) [serum creatinine, electrolytes & BUN]
- Baseline **ophthalmological exam** (check for glaucoma)

DOSING

Oral, Rectal:

- 10mg po tid or qid (up to q4h) regularly or PRN dosing, substitute suppository if frequent emesis
- 10mg po pre-chemotherapy for low to moderately emetogenic chemotherapy
- Injection:**
- 10mg IV pre-chemotherapy if oral route not appropriate

Pediatric

Oral, Rectal:

- >10Kg- 0.4mg/Kg/24 hrs in 3-4 divided doses, OR
- 9-14Kg- 2.5mg q12-24h PRN, Maximum 7.5mg/day
- 14-18Kg- 2.5mg q8-12h PRN, Maximum 10mg/day
- 18-39Kg- 2.5mg q8h or 5mg q12h PRN, Maximum 15mg/day

IM:

- 0.1-0.15 mg/Kg/dose (0.13mg/Kg usual dose)
- IV. Not recommended for children <10Kg or <2 yrs

SIGNIFICANT INTERACTIONS

CNS-depressants
anticonvulsants
Lithium
Metrizamide

PHARMACEUTICAL CONSIDERATIONS

Tablets: 5mg or 10mg prochlorperazine (as bimeleate) in orange tablets. Tartrazine-free.

Suppositories: 10mg prochlorperazine. Store in cool place.

Injectable: 10mg/2mL prochlorperazine (as mesylate). Protect from light. Discard if markedly discoloured. Avoid getting solution on skin or hands because of possibility of contact dermatitis developing.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-

Injection-Basic Level;

Oral- Take Home Prescription

CDHA Status	Formulary
Pharmacare Status	Formulary

RALTITREXED

(Antineoplastic Agent)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Tomudex®

Vials of 2mg for reconstitution

MECHANISM OF ACTION

Raltitrexed is a folate antagonist that inhibits thymidylate synthase, blocking purine synthesis. This results in an overall inhibition of DNA, RNA, and protein synthesis.

PHARMACOKINETICS

Oral Absorption

no information

Distribution

transported into cells via reduced folate carrier (RFC)

cross blood brain barrier? No information

Vd- no information PPB- 93%

Metabolism

extensively polyglutamated by the enzyme folyl polyglutamate synthetase (FPGS) to polyglutamate forms (intracellular); little or no systemic metabolism of the drug metabolite(s): active- polyglutamate forms (more potent inhibitors)
inactive- no information

Excretion

renal- three phases, slow elimination phase; feces (15%)

Urine: 50% unchanged

Elimination $t_{1/2}$ - 1.3-2.6 hours

Terminal $t_{1/2}$ - 8-168 hours

Cl- 51.6 mL/min; renal Cl 25.1 mL/min

DOSING

Intravenous:

3 week:

- 3 mg/m² (range 0.75-3 mg/m²) IV for one dose on day 1
- once a dose reduction has been made, all subsequent doses should be given at the reduced dose level

Concurrent radiation:

5-6 weeks

- investigational, 2.6 mg/m² IV for one dose on days 1 and 22 concurrent with radiation for 5-6 weeks
- (total dose per cycle 5.2 mg/m²)

Pediatric

- Safety & effectiveness not established

IV COMPATIBILITY

sodium chloride 0.9%

dextrose 5%

ROUTES

intravenous infusion over 15 minutes

ADMINISTRATION

- Mix in 50mL (to 100mL) minibag (Normal Saline, 5% Dextrose); Infuse over 15 minutes

EXTRAVASATION HAZARD

none

ANTIEMETIC RISK

LOW RISK (Less than 10% of patients)

- No routine antiemetic pre or post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

SIGNIFICANT INTERACTIONS

NSAIDs

Avoid leucovorin calcium (folinic acid), folic acid and vitamin preparations containing these agents during raltitrexed therapy as they may interfere with drug activity

INDICATIONS AND OTHER USES

- Colorectal cancer

OTHER ONCOLOGY USES

Breast cancer

Gastroesophageal cancer

CONTRAINDICATIONS

- uncontrolled diarrhea
- severe hepatic impairment and/or renal impairment

Continued Next Page...

RALTITREXED

DRUG

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET	(hours to days)	EARLY ONSET	(days to weeks)
diarrhea (14%)		<i>myelosuppression</i>	
nausea/vomiting (13%)		stomatitis, mucositis, anorexia	
heartburn		elevated liver enzymes	
		flu-like symptoms- fever, asthenia,	
		malaise, fatigue	
		alopecia, skin rash	
		cardiac rhythm or function disorders	

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- Baseline & regular **liver function tests** (if severe organ failure suspected) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- Baseline **renal function tests** (if severe organ failure suspected) [serum creatinine, electrolytes & BUN]
- **Clinical assessment of stomatitis**: oral examination upon patient complaint of a sore mouth

• Routine assessment of **Diarrhea**, at each clinic visit and telephone reinforcement

DIARRHEA	STOMATITIS (Pharyngitis)
0. None	0. None
1. Increase of 2-3 stools/day over pretreatment	1. Painless ulcers, erythema, or mild soreness in the absence of lesions
2. Increase of 4-6 stools/day or nocturnal stools	2. Painful erythema, edema, or ulcers, but can eat or swallow
3. Increase of 7-9 stools/day, incontinence, malabsorption	3. Painful erythema, edema, or ulcers requiring IV hydration
4. Increase of ≥ 10 stools/day, grossly bloody diarrhea, need for parenteral nutrition support	4. Severe ulceration or requires parenteral or enteral nutritional support or prophylactic intubation

Rated at each visit

Rated at each visit

Continued Next Page...

RALTITREXED

DOSE ADJUSTMENT CRITERIA

Renal Failure:

Measure or calculate creatinine clearance from serum creatinine (Suggested action)

- If CrCl = 55-65 mL/min, reduce to **75%** dose.
- If CrCl = 25-54 mL/sec, reduce to **25-54%** dose (%age dose = CrCl in mL/min);
- If Cr Cl < 25 mL/min, **OMIT** dose

Hepatic Failure: (Suggested action)

- If pre-existing hyperbilirubinemia, no dosage change
- If bilirubin increase suspected to be related to drug, delay dosage until resolved

Gastrointestinal Toxicity:

- If Grade 2 diarrhea or stomatitis, **reduce to 75% dose**
- If Grade 3 diarrhea or stomatitis, **reduce to 50% dose**
- If Grade 3 diarrhea with severe neutropenia ($<0.5 \times 10^9/L$) or thrombocytopenia ($<10 \times 10^9/L$), **OMIT** dose
- If Grade 4 diarrhea or stomatitis, **OMIT** dose

PHARMACEUTICAL CONSIDERATIONS

Injection:

2 mg vial (as the disodium salt). Store at room temperature. Protect from light. Reconstitute powder with 4 mL SWI to a final concentration of 0.5 mg/mL.

Reconstituted solution for injection:

Chemically stable for 24 hours at room temperature exposed to ambient light, however, it is recommended that raltitrexed be refrigerated to avoid bacterial contamination.

Diluted solution for infusion:

Dilute in 50-250 mL NS or D5W. Chemically stable for 24 hours at room temperature exposed to ambient light. If not used promptly, it is recommended that raltitrexed be refrigerated to avoid bacterial contamination.

Compatibility: It is recommended that raltitrexed not be mixed with other drugs.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Basic Level, Indication restriction-
Provincial Cancer Drug Formulary
CDHA Formulary / Status Formulary-
Restricted
Pharmacare Formulary Status
Colorectal cancer
(5-fluorouracil/leucovorin therapy is
contraindicated)

RITUXIMAB

DRUG

(Antineoplastic Agent, Monoclonal Antibody)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Rituxan® Vials with 100mg/10mL, 500mg/50mL for further dilution

MECHANISM OF ACTION

Rituximab is a monoclonal antibody directed against the CD20 antigen on B-lymphocytes. CD20 regulates cell cycle initiation; and, possibly, functions as a calcium channel. It binds to the antigen on the cell surface, activating complement-dependent cytotoxicity; and to human Fc receptors, mediating cell killing through an antibody-dependent cellular toxicity.

PHARMACOKINETICS

Oral Absorption

no information

Distribution

no information, excretion in breast-milk unknown

cross blood brain barrier? no information
Vd, PPB- no information

Metabolism

no information

Excretion

uncertain, may undergo phagocytosis and catabolism in the RES

t_{1/2} proportional to dose: 59.8 hours after first infusion; 174 hours after the fourth infusion

IV COMPATIBILITY

sodium chloride 0.9% OR dextrose 5% ONLY

ADMINISTRATION

- Premedicate with Acetaminophen 650mg (2 tabs) and Diphenhydramine 50mg PO
- Mix in Normal Saline or 5% Dextrose to a final concentration of 1 to 4mg/mL (3mg/mL used as standard dilution at QEII HSC- see NOTE)
- First infusion: start at 50mg/hour; if tolerated, increase every 30 minutes by increments of 50mg/hour to a maximum rate of 400mg/hour
- Subsequent infusions: Start at 100mg/hour and increase every 30 minutes by 100mg/hour increments to 400mg/hour as tolerated
- Observe closely for infusion-related symptoms; use supportive care measures as needed (IV saline, diphenhydramine, epinephrine, corticosteroid, acetaminophen, bronchodilators- these agents should be immediately available at the site)
- After an interruption for a severe reaction, the infusion can be resumed at a 50% reduction in rate once the symptoms have resolved.
- DO NOT give by IV push or bolus dose
- Patients taking anti-hypertensive drugs should be instructed to hold their medications 12 hours prior to an infusion.

ROUTES

intravenous infusion (over several hours); gradual rate increases to avoid hypersensitivity reactions
never undiluted or by rapid IV injection

DOSING

Intravenous:

1 week

- 375 mg/m² for one dose on day 1, repeat weekly for 4 weeks (days 1, 8, 15 & 22)

3 weeks

- 375 mg/m² for one dose within 72 h before or after day 1 of CHOP chemotherapy regimen

Bone marrow transplant:

- 375 mg/m² for one dose on day 0 (ie, day of bone marrow reinfusion)

Pediatric

- Safety & effectiveness not established

Other dosing may be indicated

Continued Next Page...

RITUXIMAB

SIDE EFFECTS

side effects in **bold, italic type** are common

* may be life-threatening

IMMEDIATE ONSET (hours to days)

- Infusion-related reactions***: fever (49%) & chills/rigors (32%) within 30 minutes to 2 hours. Other symptoms include hypotension, nausea, urticaria, fatigue, headache, pruritis, dyspnea, flushing of face, rigor, bronchospasm, angioedema, sensation of tongue or throat swelling, rhinitis, vomiting, pain at disease sites
- Pulmonary Events**: Hypoxia, pulmonary infiltrates, acute respiratory failure, bronchospasms, dyspnea, edema
- tumor lysis syndrome**: hyperuricemia, hyperkalemia, hypocalcemia, acute renal failure, elevated LDH, high fevers
- cardiovascular events**: hypotension, cardiac arrhythmias, cardiac failure, cardiogenic shock, nausea/vomiting

EARLY ONSET (days to weeks)

- myelosuppression (rare and mild): thrombocytopenia, neutropenia, anemia

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Observation for **hypersensitivity reaction** during and for 30 minutes after injection (emergency treatment readily available)
- For patients, who develop clinically significant arrhythmias during administration, continuous monitoring during subsequent administrations

SUGGESTED CRITERIA

- Routine **peripheral blood tests** for CD20+ cells
- Baseline & periodic **cardiac function tests** (Echo RNA and/or MUGA scans) for all patients with cardiac risk factors
- HYPERSENSITIVITY/ALLERGY**

0 None

1 Transient rash, fever <38°C

2 Urticaria, fever ≥38°C, mild bronchospasm

3 Serum sickness, bronchospasm, requires parenteral medications

4 Anaphylaxis

Rated In Response To Patient Reaction

INDICATIONS AND OTHER USES

- Lymphoma, non-Hodgkin's
- OTHER ONCOLOGY USES**
- Lymphoma, transplant-related*
- B-cell purging in autologous bone marrow transplant*

ANTIEMETIC RISK

LOW RISK (Less than 10% of patients)

- No routine antiemetic pre-chemotherapy or post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

CONTRAINDICATIONS

- known type I hypersensitivity to murine (mouse) proteins
- caution in patients with very large tumour burden
- history of cardiac conditions, incl Angina, arrhythmias
- pregnancy
- antihypertensive medications, bronchodilators

EXTRAVASATION HAZARD

possibly yes

Continued Next Page...

RITUXIMAB

DRUG

PHARMACEUTICAL CONSIDERATIONS

Injection

100 mg and 500 mg vials, each mL contains 10 mg rituximab. For single use only, unused portions must be discarded. Store under refrigeration. Protect from light. Diluted solution for infusion.

Dilute prior to infusion using NS or D5W to a final concentration of 1-4 mg/mL. Stable for 24 hours refrigerated and 36 hours at room temperature. Mix by inverting bag gently to avoid foaming.

Compatibility

It is recommended that rituximab not be mixed with other drugs.

NOTE: Potentially fatal serious infusion related events can occur. In a 13 month period, the manufacturer reported 70 cases of serious infusion related events (out of estimated 12,000 to 14,000 patients) 8 of which were fatal (i.e. <1 per 1000 patients).

DOSE ADJUSTMENT CRITERIA

Infusion-related reactions

Reduce infusion rate or stop.

May restart infusion at 50% of previous rate upon improvement of symptoms.

Tumor Lysis Syndrome or pulmonary infiltration.

Discontinue infusion

Treat symptoms with diphenhydramine or acetaminophen plus bronchodilators or intravenous sodium chloride, if indicated. Resume at a 50% rate when symptoms have completely resolved.

Cardiovascular events

If serious or life-threatening, **discontinue infusion!**

SIGNIFICANT INTERACTIONS

none known

GUIDELINES

Visit the **Cancer Care Nova Scotia** website (www.cancercare.ns.ca) for the guideline on Rituximab for non-Hodgkin's lymphoma.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Intermediate Level. *Indication restriction-* Provincial Cancer Drug Formulary

CDHA Status: Non-Formulary-
Restricted to Guideline Indications
Pharmacare Status: Non-Formulary

RITUXIMAB

NOTE

Mixing and administration to reach a fixed Rituximab concentration

To reach a final concentration of 3 mg/mL Rituximab:

BSA (mg/m ²)	Dose (mg)	Rituxan (mL*)	Diluent (mL)	Total Volume (mL)	For this dosage rate (mg/hr)							
					50	100	150	200	250	300	350	400
					Use the following INFUSION RATE (mL/hr)							
1.3	488	49	114	163	17	33	50	67	83	100	117	133
1.4	525	53	124	177	17	33	50	67	83	100	117	133
1.5	563	56	131	187	17	33	50	67	83	100	117	133
1.6	600	60	140	200	17	33	50	67	83	100	117	133
1.7	638	64	149	213	17	33	50	67	83	100	117	133
1.8	675	68	159	227	17	33	50	67	83	100	117	133
1.9	713	71	166	237	17	33	50	67	83	100	117	133
2.0	750	75	175	250	17	33	50	67	83	100	117	133
2.1	788	79	184	263	17	33	50	67	83	100	117	133
2.2	825	83	194	277	17	33	50	67	83	100	117	133

TAMOXIFEN

(Antineoplastic Agent; Hormone (Antiestrogen))

Revision Date: Feb 03

DRUG

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Nolvadex® Tablets with 10mg, 20mg Tamoxifen

Generic products available

MECHANISM OF ACTION

Tamoxifen competes with estrogen for estrogen receptors on tumor cells, inhibiting estrogen's ability to stimulate tumor growth, and decreasing DNA synthesis. Inhibition of messenger RNA by the tamoxifen-estrogen receptor complex within tumor cells is also postulated. Cells tend to accumulate in the G0 and G1 phase of the cycle. Tamoxifen appears to be more a cytostatic, rather than cytotoxic, agent.

PHARMACOKINETICS

Oral Absorption

well absorbed orally

Distribution

high concentrations in uterus, endometrium, breast, prostate and ovary, enters breast-milk

cross blood brain barrier? no information

Vd- no information PPB- 99%

Metabolism

by hepatic microsomal enzyme oxidation system, causes autoinhibition of metabolism; major metabolites:

Desmethyltamoxifen, 4-hydroxytamoxifen

metabolite(s): inactive- yes

active- N-desmethyltamoxifen

Excretion

secreted in bile, undergoes enterohepatic circulation, slowly excreted in feces (26% to 51%), renal (9% to 13%)

Urine: <1%

t_{1/2} α - 7-14 hours after single dose

t_{1/2} β - 7 days at steady state; metabolites 10-20 days

Elimination t_{1/2} > 7 days

ROUTES

oral

INDICATIONS AND OTHER USES

- Breast cancer (treatment or prevention)

OTHER ONCOLOGY USES

Brain tumours

Endometrial cancer

Malignant melanoma

Pancreatic cancer (post-menopausal women)

Prostate cancer

CONTRAINDICATIONS

- known hypersensitivity to tamoxifen
- history of thromboembolic problems
- pregnancy and breast feeding

DOSING

Oral:

- daily: 20 mg po
- daily: 20 mg/m² po
- bid: 10-20 mg po
- qid: 40 mg po x 7 days, then 20 mg po bid (for malignant melanoma)

Adjuvant therapy (breast):

- 5 years
- Advanced disease:
- as long as disease responding

Adequate trial:

- 1-4 months
- bone metastases may take several months to respond

Pediatric:

- Safety & effectiveness not established

SIGNIFICANT INTERACTIONS

allopurinol, aminoglutethimide, cyclophosphamide, irradiation, medroxyprogesterone, melphalan, phenobarbital, theophylline, warfarin, other antineoplastic agents

Cytochrome P450 3A Substrate

Continued Next Page...

TAMOXIFEN

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)

nausea and vomiting (25%)
distaste for food

DELAYED/LATE ONSET (weeks- years)

- * blood clots (infrequent, pulmonary emboli or thrombosis)
- mental depression (rare)
- eye problems (more common with high doses, retinopathy, corneal opacities)
- * endometrial cancer (rare) and uterine cancer (rare)

EARLY ONSET (days to weeks)

hot flushes (25%)
headache (rare)

- * flare response (transient increase in bone or tumour pain and/or hypercalcemia)
- menstrual irregularities
- swelling of extremities (edema)
- vaginal discharge or bleeding (rare)
- vulvar itching (rare, pruritis vulvae)
- dizziness (rare)
- * low WBC, platelets (rare, transient myelosuppression)
- skin problems (rare, rash, dermatomyositis)
- * liver problems (elevated liver function tests, rare, transient, liver damage, rare)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- * Clinical assessment- endometrial hyperplasia/ neoplasia

SUGGESTED CRITERIA

NO ADDITIONAL TOXICITY RATINGS

PHARMACEUTICAL CONSIDERATIONS

Tablets

10 mg, 20 mg (as the citrate salt); store at room temperature, protected from heat and light. Nolvadex®/Nolvadex-D® tablets are alcohol-, sodium- and tartrazine-free. Tamoplex and Apo-Tamox are gluten- and tartrazine-free. Novo-Tamoxifen® is tartrazine-free.

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level. Take Home
Prescription (NOTE: Use of pre-
printed Physician Standing Order is
recommended for initial treatment)

CDHA Status	Formulary
Pharmacare Status	Formulary

TEMOZOLOMIDE

(Antineoplastic Agent, Alkylating Agent)

Revision Date: Feb 03

DRUG

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Temodal® Capsules with 5mg, 20mg, 100mg, 250mg

Temozolomide

MECHANISM OF ACTION

Like DTIC, temozolomide is converted to the active alkylating metabolite MTIC.

Unlike DTIC, however, this conversion is spontaneous, nonenzymatic, and occurs under physiologic conditions in all tissues to which the drug distributes.

PHARMACOKINETICS

Oral Absorption

rapidly absorbed, often 100% bioavailability; influence of food <10% effect on absorption extent, but administer without food

Distribution

extensively distributed; excretion in breast-milk unknown
cross blood brain barrier? Significant penetration (35-39%)

Vd 0.4 L/kg (parent compound)

PPB low (10-20%)

Metabolism

Hydrolysis at pH 7.4- produces the cytotoxic metabolite 3-methyl-(triazene-1-yl)-imidazole-4-carboxamide (MTIC).

MTIC decomposes to 5-amino-imidazole-4-carboxamide (AIC)- (dose independent)

metabolite(s): active- MTIC, methyldiazonium species
inactive- no information

Excretion

rapidly eliminated by pH-dependent degradation to MTIC, followed by degradation to 4-amino-5-imidazole carboxamide (AIC= a natural constituent in urine); renal clearance only accounts for 5% to 7% of total clearance

Urine: <10% unchanged drug

CI 11.76L/hr

ROUTES

oral

DOSING

Oral:

4 weeks:

- 150 mg/m² (range 100-200 mg/m²) PO once daily for 5 consecutive days starting on day 1 (total dose per cycle = 750 mg/m² [range 500-1000 mg/m²])
- Round dose to the nearest 5 mg.
- Administer with food or on an empty stomach, in the morning. Administering on an empty stomach (one hour before or after breakfast) may help reduce nausea.

Concurrent radiation:

- investigational, 75 mg/m² orally once daily for 42-45 days with concurrent radiation for 6-7 weeks

Pediatric: Same as adult dosing

Other dosing may be indicated in specific regimens

SIGNIFICANT INTERACTIONS

food, valproic acid, other alkylating agents

INDICATIONS AND OTHER USES

- Astrocytoma
- Glioblastoma

OTHER ONCOLOGY USES

Brain metastases from solid tumours
Melanoma

CONTRAINDICATIONS

- known hypersensitivity to dacarbazine (DTIC)
- pregnancy
- severe myelosuppression

Continued Next Page...

TEMOZOLOMIDE

SIDE EFFECTS

* may be life-threatening

side effects in **bold**, *italic* type are common

IMMEDIATE ONSET

(hours to days)

nausea/vomiting
headache

EARLY ONSET (days to weeks)

* **myelosuppression**
fatigue
constipation

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment & nadir blood counts on Day 22

SUGGESTED CRITERIA

NO ADDITIONAL TOXICITY RATINGS

DOSE ADJUSTMENT CRITERIA

Myelosuppression:

If $ANC < 1.0 \times 10^9/L$ or $PLT < 50 \times 10^9/L$ during any cycle, the next cycle must be reduced

PHARMACEUTICAL CONSIDERATIONS

Capsules: 5 mg, 20 mg, 100 mg and 250 mg; inactive ingredients include lactose. Store at room temperature. Protect from moisture.

GUIDELINES

Visit the **Cancer Care Nova Scotia** website (www.cancercare.ns.ca) for the guideline on Temozolomide for malignant glioma

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Community Level: Prescription
ordered on preprinted Physician
Standing Order as per treatment
guidelines; *Indication restriction-*
Provincial Cancer Drug Formulary
CDHA Status Non-Formulary
Pharmacare Status Non-Formulary
(Prescriber must write letter of
request for coverage)
NOTE: It is recommended to limit
ordering of this medication to
preprinted Physician Standing Order
form, for patient safety

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Hycamptin® Vials with 4mg for reconstitution (light yellow/green solution)

MECHANISM OF ACTION

Topotecan is a semisynthetic derivative of camptothecin, which inhibits topoisomerase-1. Inhibition of topoisomerase-1 leads to arrest of DNA replication and ultimately to cell death.

PHARMACOKINETICS

Oral Absorption

Bioavailability: 32-44%

Distribution

evenly distributed between plasma and blood cells. Significant quantities in cerebrospinal fluid; enters breast-milk cross blood brain barrier? Yes (30%)
PPB- 35% Vd- 130L- decreased by 25% in patients with moderate renal impairment

Metabolism

undergoes reversible pH-dependent hydrolysis of the active lactone moiety- open-ring hydroxyacid (if pH<4, lactone form; at physiologic pH, hydroxyacid)
small quantities of N-demethylated derivative via hepatic microsomal enzymes
metabolite(s):
inactive- open-ring hydroxyacid

Excretion

renal 45% over 24 hours; some by biliary route

Urine: yes

t½ - 2-3 hrs if normal renal & hepatic function, 5 hrs if renal impairment; slight increase if hepatic function impairment

Cl- 1030mL/min (27L/hour/m2) if normal renal & hepatic function (25% higher in ♂ than ♀)

IV COMPATIBILITY

sterile water

ROUTES

intravenous infusion over 30 minutes or 24 hours

ADMINISTRATION

- Mix in 50-100mL minibag (Normal Saline, 5% Dextrose); Infuse over 30 minutes

EXTRAVASATION HAZARD

mild local reactions (erythema)

ANTIEMETIC RISK

INTERMEDIATE RISK (10-30% of patients)

- Use a dexamethasone pre-chemotherapy and a dopamine receptor antagonist PRN post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

SIGNIFICANT INTERACTIONS

blood dyscrasia-causing medications, bone marrow depressant agents, cisplatin, cyclosporin, docetaxel, filgrastim, probenecid, phenytoin, radiation therapy
other immunosuppressants (e.g. azathioprine, steroids, etc.)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment

SUGGESTED CRITERIA

- Baseline renal function tests (if failure suspected) [serum creatinine, electrolytes & BUN]

Continued Next Page...

TOPOTECAN

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)
nausea, vomiting (60-70%)

EARLY ONSET (days to weeks)

* ***myelosuppression***
alopecia (59%)
joint pain, headache
diarrhea (42%)
stomatitis

DOSING

Intravenous:

3 weeks:

- 1.5 mg/m² (range 0.75-2 mg/m²) IV once daily for 5 consecutive days starting on day 1
- (total dose per cycle 7.5 mg/m² [range 3.75-10 mg/m²])

3-4 weeks:

- 1.25 mg/m²/day IV over 24 hours for 5 consecutive days
- (total dose per cycle 6.25 mg/m²)

4-6 weeks:

Other dosing may be indicated

- 2 mg/m²/day (range 1-2 mg/m²/day) IV over 24 hours for 5 consecutive days starting on day 1 every 4-6 weeks until remission, then every 4-8 weeks (total dose per cycle 10 mg/m² [range 5-10 mg/m²])

Pediatric

Intravenous:

3 weeks:

- 2 mg/m²/day (range 1.5-2 mg/m²/day) IV once daily for 5 consecutive days starting on day 1
- (total dose per cycle 10 mg/m² [range 7.5-10 mg/m²])

INDICATIONS AND OTHER USES

- Ovarian cancer
- Lung cancer, small cell

OTHER ONCOLOGY USES

Gliomas

Leukemia, acute myelogenous

Leukemia, chronic myelomonocytic

Lung cancer, non-small cell

Multiple myeloma

Myelodysplastic syndrome

Neuroblastoma

Pancreatic cancer

Retinoblastoma

Rhabdomyosarcoma

Sarcoma, Ewing's

DOSE ADJUSTMENT CRITERIA

Renal failure (*Suggested action*)

- 1 If CrCl = 20-40 mL/min, give **50%** dose,
- 2 If CrCl < 20 mL/min, **OMIT** dose

CONTRAINDICATIONS

- severe renal function impairment (creatinine clearance <20mL/min)
- pregnancy, breast feeding

Continued Next Page...

TOPOTECAN

PHARMACEUTICAL CONSIDERATIONS

Injection:

4 mg vial, (as free base). Store at room temperature. Protect from light. Reconstitute powder with 4 mL of SWI to yield a topotecan concentration of 1 mg/mL.

Reconstituted solution for injection:

Reconstituted solution is stable for up to 24 hours at room temperature or under refrigeration. However, since the vials contain no preservatives, it is recommended that the solution be used immediately after reconstitution. If not used immediately, the reconstituted solution should be refrigerated and discarded after 24 hours.

Diluted solution for infusion:

Must be further diluted with D5W or NS to final concentration of 0.02-0.5 mg/mL. 11 Diluted solution is chemically and physically stable for 24 hours at room temperature and for 7 days, refrigerated under ambient lighting condition. However, the manufacturer recommends the admixture be used within 24 hours since the solution does not contain preservatives. 11 When topotecan is reconstituted and diluted with bacteriostatic water for injection at concentrations of 0.01 mg/mL and 0.5 mg/mL in Pharmacia Deltec cassettes, the solution is chemically stable for 21 days at room temperature and under refrigeration.

Bacterial challenge:

Topotecan 0.01 mg/mL diluted in NS did not exhibit an antimicrobial effect on the growth of four organisms inoculated into the solution. Diluted solutions should be stored under refrigeration whenever possible and that the potential for microbiological growth be considered when assigning expiration periods.

Compatibility:

The following are compatible via Y-site injection: carboplatin, cisplatin, cyclophosphamide, doxorubicin, etoposide, gemcitabine, granisetron, ifosfamide, metoclopramide, ondansetron, prochlorperazine, paclitaxel, vincristine.

Incompatibility:

The following are incompatible via Y-site injection: dexamethasone, fluorouracil, methylprednisolone, mitomycin.

GUIDELINES

Visit the **Cancer Care Nova Scotia** website (www.cancercare.ns.ca) for the guideline on Topotecan for ovarian cancer

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Intermediate Level; *Indication*
restriction- Provincial Cancer Drug
Formulary
CDHA Status Formulary- Restricted
Pharmacare Status Non-Formulary

TRASTUZUMAB

(Antineoplastic Agent; Monoclonal Antibody)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Herceptin™ Vials with 440mg for reconstitution

MECHANISM OF ACTION

Trastuzumab binds to the extracellular domain of the human epidermal growth factor receptor (HER2) protein, mediating an antibody-dependent cellular toxicity in cells that over express the HER2 protein.

PHARMACOKINETICS

Oral Absorption

no information

Distribution

no information; excretion in breast-milk unknown

cross blood brain barrier? no information

Vd- 44mL/Kg PPB- no information

Metabolism

no information

Excretion

nonlinear- increased doses→increased half-life & increased clearance

Urine: no information

t½ 1-32 days (dose-dependant); mean= 5.8 days

Cl- no information

DOSING

Intravenous:

1 week:

- 4 mg/kg IV loading dose on day 1 of first cycle, then 2 mg/kg IV for one dose on day 1 of each subsequent cycle
- If treatment has been stopped for more than 2 cycles, then patient may need to be restarted with loading dose.

3 weeks:

- 8 mg/kg IV loading dose on day 1 of first cycle, then 6 mg/kg IV for one dose on day 1 for each subsequent cycle

Pediatric: No pediatric indications

Other dosing may be indicated

IV COMPATIBILITY

bacteriostatic water for injection, sodium chloride 0.9% ONLY

ROUTES

intravenous infusion over short period

ADMINISTRATION

- Premedicate with Acetaminophen 2 tabs and Diphenhydramine 50mg PO
- Mix in 250mL bag Normal Saline (NOT 5% Dextrose); Infuse loading dose over 90 minutes, observe for 60 minutes; Infuse maintenance doses over 30 minutes, observe for 30 minutes, if the loading dose is adequately tolerated. If the patient does not adequately tolerate the loading dose, continue with a 90 minute infusion followed by a 60 minute observation period. Infusions may be temporarily interrupted and restarted later if symptoms subside.
- DO NOT give by IV push or bolus dose

EXTRAVASATION HAZARD

no information

ANTIEMETIC RISK

LOW RISK (Less than 10% of patients)

- No routine antiemetic pre-chemotherapy or post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

Continued Next Page...

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)

Infusion-related reactions: (40% during first infusion, less frequent with subsequent infusions) chills, fever, pain, rigor, headache, dizziness, dyspnea, hypotension, wheezing, bronchospasm, reduced oxygen saturation, respiratory distress, rash, asthenia
nausea/vomiting

EARLY ONSET (days to weeks)

* **Cardiac Adverse Events:** dyspnea, edema

→ **increased incidence observed in combination with chemotherapy (esp. anthracycline or cyclophosphamide)**

Pulmonary effects- increased cough

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Baseline & periodic **cardiac function tests** (Echo RNA and/or MUGA scans) for all patients with cardiac risk factors

SUGGESTED CRITERIA

- Observe for **infusion-related reactions** for at least 1 hour after completion of first infusion and 30 minutes after 2nd and subsequent infusions, if well tolerated.

INDICATIONS AND OTHER USES

- Metastatic breast cancer (in which tumors over express the Human Epidermal Growth Factor Receptor 2 (HER2) protein; as single agent treatment for relapse following one or more chemotherapy regimens for metastatic disease and as combination therapy with paclitaxel for previously untreated metastatic disease)

CONTRAINDICATIONS

- known hypersensitivity to trastuzumab, chinese hamster ovary (CHO) cell proteins or other components of product

DOSE ADJUSTMENT CRITERIA

Infusion-related reactions:

If serious: **discontinue the infusion**
Monitor until resolution of symptoms.

Treat serious reactions with supportive therapy such as oxygen, beta-agonists and corticosteroid

If less serious: acetaminophen for fever and/or temporarily interrupt infusion or **slow infusion rate** until the symptoms are resolved.

Cardiac adverse effects:

Discontinue treatment in patients who develop a clinically significant decrease in left ventricular function.

SIGNIFICANT INTERACTIONS

anthracyclines, cyclophosphamide, (paclitaxel), warfarin

→ **higher incidence and severity of cardiac dysfunction**

Continued Next Page...

TRASTUZUMAB**PHARMACEUTICAL CONSIDERATIONS**Injection:

440 mg vial with 20 mL vial of bacteriostatic water for injection (BWI) containing benzyl alcohol. Store under refrigeration.

Reconstitute powder with 20 mL of BWI or SWI to a final concentration of 21 mg/mL.

Reconstituted solution for injection:

stable for 28 days if reconstituted with BWI and refrigerated. Do not freeze reconstituted solution. If reconstituted with SWI, solution must be used immediately and any unused portion should be discarded.

Diluted solution for infusion:

Dilute in 250 mL NS, mix by inverting bag gently to avoid foaming. Do not mix with D5W. Stable for 24 hours at room temperature up to 30°C. If not used promptly, it is recommended that the admixture be refrigerated to avoid bacterial contamination.

Compatibility:

It is recommended that trastuzumab not be mixed with other drugs.

Incompatibility:

dextrose is incompatible via Y-site injection or in the same infusion solution.

GUIDELINES

Visit the **Cancer Care Nova Scotia** website (www.cancercare.ns.ca) for the guideline on Trastuzumab for advanced breast cancer

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Intermediate Level for initial
treatment(s), then Basic Level if no
reactions, *Indication restriction-*
Provincial Cancer Drug Formulary
CDHA Status Formulary- Restricted
Metastatic Breast Cancer
Pharmacare Status Non-Formulary

VINBLASTINE

(Antineoplastic Agent; Vinca Alkaloid)

Revision Date: Feb 03

DRUG

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Velbe® Vials with 10mg for reconstitution
Generic products available: Vials with 10mg/10mL

MECHANISM OF ACTION

Vinblastine binds to tubulin, inhibiting microtubule formation. The resulting metaphase arrest causes disruption of the mitotic spindle. It may also interfere with nucleic acid and protein synthesis by blocking glutamic acid utilization. It is specific for the M and S phases of the cell cycle.

PHARMACOKINETICS

Oral Absorption

oral absorption erratic

Distribution

rapid and extensive binding to tissues and to formed elements of peripheral blood; enters breast-milk
cross blood brain barrier? trace
Vd- 27.3 L/kg PPB- 99%

Metabolism

metabolized in liver
metabolite(s) active-
desacetylvinblastine inactive- yes

Excretion

disposition described by a three compartment model; slowly excreted in urine and feces; feces 10%
Urine 13.6% to 23.3% (1% as unchanged drug)
 $t_{1/2\alpha}$ <5 minutes
 $t_{1/2\beta}$ 0.9-1.7 hours
 $t_{1/2\gamma}$ 19-25 hours
Cl- 0.74 L/kg/h

IV COMPATIBILITY

normal saline, dextrose 5%

ROUTES

direct IV (preferred)
intermittent IV (in 100 mL over 20-30 minutes; in >250 mL over 3-8 hours, VAD preferred)
continuous IV (via VAD)

ADMINISTRATION

- Quick push through sidearm of free flowing IV (5% Dextrose, Normal Saline); Inject over 1 minute (*administering nurse should be certified to administer IV push chemotherapy agents*)
- May be given by direct IV push, followed by a Normal Saline flush, if no IV line has been set up
- Mix in 50mL minibag (Normal Saline, 5% Dextrose); Infuse over 15-30 minutes

INDICATIONS AND OTHER USES

- Breast cancer
- Hodgkin's disease
- Kaposi's sarcoma
- Testicular cancer
- Choriocarcinoma
- Histiocytosis X
- Mycosis fungoides
- Non-Hodgkin's lymphoma

OTHER ONCOLOGY USES

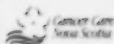
Bladder cancer
Cervical cancer
Germ cell cancer
Lung cancer, non small cell
Renal cell cancer

EXTRAVASATION HAZARD

VESICANT (tissue damage on extravasation)
Management- stop IV, aspirate, elevate limb, warm intermittent compresses
Follow Extravasation Guidelines

CONTRAINDICATIONS

- known hypersensitivity to vinblastine, or other vinca alkaloids
- pregnancy and breast feeding



VINBLASTINE

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET (hours to days)

- * anaphylaxis (rare)
- pain on injection (chemical phlebitis)
- vasoconstriction of extremities (Raynaud's syndrome, rare)
- parotid gland pain, muscle and tumour pain
- nausea and vomiting (uncommon, usually mild)
- * pulmonary toxicity (acute shortness of breath, bronchospasm)

DELAYED/LATE ONSET

infertility

EARLY ONSET (days to weeks)

- * **low WBC, RBC, platelets** (*myelosuppression*, nadir 4-9 days, recovery 7-21 days)
- hair loss (alopecia)** (common, usually mild)
- nerve problems (peripheral, cranial nerve and autonomic neuropathy)
- constipation (may be severe, autonomic neuropathy)
- bladder problems (urinary retention, autonomic neuropathy)
- mouth sores (stomatitis)
- SIADH (rare, hyponatremia, central neurotoxicity)
- increased uric acid levels (hyperurcemia)
- skin problems (photosensitivity, rare)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Neurologic toxicity ratings (Sensory) at each visit

SENSORY

- 0 No change
- 1 Mild paraesthesia, no deep tendon reflex
- 2 Mild/mod sensory loss, mod paraesthesia
- 3 Sensory loss interferes with function

Rated At Each Clinic Visit

SUGGESTED CRITERIA

- Baseline liver function tests (if liver failure suspected) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- Local Site Toxicity ratings, if incident of phlebitis

LOCAL SITE TOXICITY

- 0 None
- 1 Pain
- 2 Pain & inflammation, phlebitis
- 3 Ulceration
- 4 Plastic surgery

Upon Patient Complaint Or Clinical Event

SIGNIFICANT INTERACTIONS

erythromycin, grapefruit, interferon alfa, medroxyprogesterone, mitomycin, phenytoin, radiation, zidovudine, other antineoplastic agents
Cytochrome P450 3A substrate and 2D6 inhibitor

ANTIEMETIC RISK

LOW RISK (Less than 10% of patients)

- No routine antiemetic pre-chemotherapy or post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

Continued Next Page

VINBLASTINE

DOSING

Intravenous

- q1w: 6 mg/m² (range 3-18.5 mg/m²)
- q2w: 6 mg/m²/q3w: 5 mg/m² x 2 days
- q3w: 4.5-6 mg/m²
- q3w: 4 mg/m² days 1 and 8
- q3-4w: 1-2 mg/m²/day x 5 days by continuous infusion
- *Maximum weekly dose:*
- 18.5 mg/m²

Adequate trial: 4-12 weeks

Pediatric

Intravenous

- q1w: 6.5 mg/m²
- q2w: 6 mg/m²

Other dosing may be indicated

DOSE ADJUSTMENT CRITERIA

Hepatic dysfunction

(Recommended action)

- 1 If Bilirubin = 25-50 µmol/L or AST = 60-180 IU/L. REDUCE to 50% dose
- 2 If Bilirubin > 50 µmol/L or AST > 180 IU/L. REDUCE to 25% dose

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status:
Intermediate Level

CDHA Status

Formulary

Pharmacare Status

Formulary (red)

PHARMACEUTICAL CONSIDERATIONS

Vinblastine may be lethal if injected intrathecally. The Compendium of Pharmaceuticals and Specialties (CPS) and the United States Pharmacopeia (USP) require that vinblastine be dispensed in an overwrap bearing the statements "Do not remove covering until moment of injection. Fatal if given intrathecally. For intravenous use only."

Injection

10 mg powder and a 1 mg/mL preservative-free solution. Store both in refrigerator. For prolonged storage, protect from light. One reference states that the Lilly and Lyphomed products are stable at room temperature 14 days and up to 2 months, respectively.

Reconstitute powder with NS to a final concentration of 1 mg/mL. NS preserved with phenol or benzyl alcohol may be used. Other diluents are not recommended.

Reconstituted solution for injection

Clear, colourless solution. Vinblastine powder reconstituted with preserved NS is stable for 30 days when refrigerated.

Stability in syringes

Stable for 14 days in PVC (Monoject) syringes.

Diluted solution for infusion

Physically stable in D5W for 24 hours at room temperature, in glass or PVC containers. Stable for 5 days in NS in PVC bags and PVC syringes at 8°, 25° and 32°C.

No substantial loss in potency was observed when a 0.2 mg/mL vinblastine solution in D5W or NS was run through a 0.22 micron cellulose ester membrane (IVEX-2) filter.

Compatible with ondansetron. It is recommended that vinblastine not be mixed with other drugs.



VINCISTINE

(Antineoplastic Agent: Vinca Alkaloid)

Revision Date: Feb 03

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Oncovin®

Vials with 1mg/1mL, 2mg/2mL, 5mg/5mL

Generic products available

MECHANISM OF ACTION

Vincristine binds to tubulin, inhibiting microtubule formation. The resulting metaphase arrest causes disruption of the mitotic spindle. It may also interfere with nucleic acid and protein synthesis by blocking glutamic acid utilization. It is specific for the M and S phase of the cell cycle. It may also interfere with nucleic acid and protein synthesis by blocking glutamic acid utilization.

PHARMACOKINETICS

Oral Absorption

poor oral absorption

Distribution

rapid and extensive tissue binding, enters breast-milk

cross blood brain barrier? CSF: plasma ratio 5%, rapidly cleared from the bloodstream

Vd: 8.4 L/kg, 163-165 L/m² PPB ~75%

Metabolism

metabolized in liver, not fully characterized

metabolite(s): active, inactive- no information

Excretion

disposition described by a three compartment model, excreted into bile (80%) and feces (~30% within 24 Hours, 70% within 72 hours, 40-50% as metabolites), renal (10-20%)

Urine: 12% within 72 hours, 50% as metabolites; children: 37% within 72 hours, <1% as unchanged drug

$t_{1/2\alpha}$ - 5 minutes $t_{1/2\beta}$ - 2-3 hours

$t_{1/2\gamma}$ - 23-85 hours; 25.5 hours (children)

Cl: 146 mL/min/1.73 m²

IV COMPATIBILITY

normal saline, dextrose 5%

ROUTES

direct IV (preferred)
intermittent IV (in 50-250 mL over 0.25-2 hours, Venous Access Device preferred)
continuous IV (via Venous Access Device)

ADMINISTRATION

- Quick push through sidearm of free flowing IV (5% Dextrose, Normal Saline). Inject over at least 1 minute (*administering nurse should be certified to administer IV push chemotherapy agents*)
- May be given by direct IV push, followed by a Normal Saline flush, if no IV line has been set up
- Mix in 50mL minibag (Normal Saline, 5% Dextrose). Infuse over 15 minutes
- Mix in 1000mL bag (Normal Saline, 5% Dextrose), usually admixed with doxorubicin as a continuous infusion for 4 days (96 hours) at a dose of 0.4 mg/day
- Continuous infusion using ambulatory infusion pump. Infuse through central venous access device or PICC line, if available
- Peripheral administration of continuous infusions of vesicants are not recommended

EXTRAVASATION HAZARD

VESICANT (tissue damage on extravasation)

Management- stop IV, aspirate, elevate limb, warm intermittent compresses
Follow Extravasation Guidelines

Continued Next Page...

VINCRIStINE

SIDE EFFECTS

* may be life-threatening

side effects in **bold**, *italic* type are common

IMMEDIATE ONSET (hours to days)

nerve problems (jaw pain, peripheral neuropathy)

nausea and vomiting (uncommon, usually mild)

seizures in children, hallucinations (central neurotoxicity)

increased uric acid levels (hyperuricemia)

fever in children

* pulmonary toxicity (acute shortness of breath, bronchospasm)

DELAYED/LATE ONSET

eye problems (cranial nerve neuropathy)

EARLY ONSET (days to weeks)

hair loss (alopecia), 50%, usually mild)

nerve problems (peripheral, cranial nerve and autonomic neuropathy)

constipation (may be severe, autonomic neuropathy)

paralytic ileus (more common in children, autonomic neuropathy)

bladder problems (urinary retention,

bladder atony, autonomic neuropathy)

progressive dyspnea

* low WBC (usually mild,

myelosuppression, nadir 4-9 days,

recovery 7-21 days)

eye problems (cranial nerve neuropathy)

SIADH (rare, hyponatremia, central

neurotoxicity)

CLINICAL MONITORING

RECOMMENDED CRITERIA

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Neurologic toxicity** ratings (Sensory, Constipation) at each visit

SENSORY

- 0 No change
- 1 Mild paraesthesia, no deep tendon reflex
- 2 Mild/moderate sensory loss, moderate paraesthesia
- 3 Sensory loss interferes with function

CONSTIPATION

- 0 No change
- 1 Mild
- 2 Moderate
- 3 Severe
- 4 Ileus >96 hours

Rated At Each Clinic Visit

SUGGESTED CRITERIA

- **Serum electrolytes and serum uric acid levels** (if symptomatic of hyperuricemia/gout)
- **Baseline liver function tests** (if liver failure suspected) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- **Local Site Toxicity ratings**, if incident of phlebitis

LOCAL SITE TOXICITY

- 0 None
- 1 Pain
- 2 Pain & inflammation, phlebitis
- 3 Ulceration
- 4 Plastic surgery

Upon Patient Complaint Or Clinical Event

VINCISTINE

INDICATIONS AND OTHER USES

- Acute lymphocytic leukemia
- Ewing's sarcoma
- Hodgkin's disease
- Lung cancer, small cell
- Non-Hodgkin's lymphoma
- Rhabdomyosarcoma
- Wilm's tumour
- Brain tumours
- Breast cancer
- Cervical cancer
- Colorectal cancer
- Malignant melanoma
- Neuroblastoma
- Osteogenic sarcoma
- Soft tissue sarcoma

OTHER ONCOLOGY USES

Chronic lymphocytic leukemia
Chronic myelogenous leukemia
Hepatoblastoma in children
Kaposi's sarcoma
Multiple myeloma
Testicular cancer

DOSING

Intravenous

- q1w: 1.0-1.4 mg/m²
- q2w: 1-2 mg
- q4w: 0.4 mg/day x 4 days as intermittent or continuous infusion
- q4w: 0.25-1 mg/m²/day x 5 days as continuous infusion

Pediatric

Intravenous:

- q1w: 1-2 mg/m² (maximum single dose 2 mg)
- q1w: 0.03-0.05 mg/kg for infants <1 m²

Other dosing may be indicated

ANTIEMETIC RISK

LOW RISK (Less than 10% of patients)

- No routine antiemetic pre-chemotherapy or post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

CONTRAINDICATIONS

- Hypersensitivity to vincristine, or other vinca alkaloids
- pregnancy and breast feeding
- demyelinating form of Charcot-Marie-Tooth Syndrome
- Cytochrome P450 enzyme substrates

SIGNIFICANT INTERACTIONS

anticonvulsant drugs, asparaginase, carbamazepine, cyclosporin, digoxin, filgrastim, irradiation, isoniazid, itraconazole, metronidazole, mitomycin, nifedipine, phenytoin, steroid hormones, verapamil, other antineoplastic agents

Cytochrome P450 3A Substrate

DOSE ADJUSTMENT CRITERIA

Hepatic dysfunction

(Recommended action)

1. If Bilirubin = 25-50 µmol/L or AST = 60-180 IU/L, REDUCE to **50%** dose
2. If Bilirubin > 50 µmol/L or AST > 180 IU/L, REDUCE to **25%** dose

Dose Capping

- Some regimens specify that the dose be capped at 2mg/dose, but others do not require capping. Doses >3mg should be confirmed with the oncologist or hematologist

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Intermediate Level

CDHA Status

Formulary

Pharmacare Status

Formulary (red)

VINCRIStINE

PHARMACEUTICAL CONSIDERATIONS

Vincristine is lethal if given intrathecally No successful antidotes have been described. The Compendium of Pharmaceuticals and Specialties (CPS) and the United States Pharmacopeia (USP) requires that vincristine be dispensed in an overwrap bearing the statements "Do not remove covering until moment of injection. Fatal if given intrathecally. For intravenous use only."

Injection

1 mg/mL solution (1 mL, 2 mL and 5 mL vials); also contains mannitol. Some products contain methyl- and propylparaben as preservatives and acetic acid/sodium acetate buffer. Store in refrigerator, protected from light, do not freeze. One reference states that vincristine vials are stable at room temperature 3 days and 30 days, for two different manufacturers respectively.

Diluted solution for infusion

May be further diluted with D5W or NS. DBL states that diluted solutions should be used within 6 hours if stored at room temperature or 24 hours when refrigerated and protected from light. Trissel reports no loss of vincristine in D5W after 24 hours storage at room temperature in glass and PVC containers. Admixtures of doxorubicin (1.4 mg/mL) plus vincristine (0.033 mg/mL) in NS or sodium chloride 0.45 % and dextrose 2.5 % injection are stable at least 4 days in PVC containers and Pharmacia cassettes at temperature 37°C.

Variable losses (up to 12%) to some filters have been reported, although filtration through Abbott IVEX in-line filters, which are specially treated with a proprietary agent, resulted in losses of only 1%.

Some mixtures with cytarabine, fluorouracil and methotrexate are reported stable in D5W for at least 8 hours at room temperature; some mixtures with doxorubicin in NS or D5W are stable for at least 24 hours. Compatible with ondansetron. It is recommended that vincristine not be mixed with other drugs. Incompatible (immediate precipitation) with furosemide.

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Navelbine® **Vials with 10mg/1mL, 50mg/5mL of pale yellow solution**
Keep under refrigeration **Protect from light**

MECHANISM OF ACTION

Vinorelbine binds to tubulin, inhibiting microtubule formation. The drug appears to be specific for mitotic microtubules: having little activity (at normal concentrations) on other microtubule classes. The resulting metaphase arrest causes disruption of the mitotic spindle. It may also interfere with nucleic acid and protein synthesis by blocking glutamic acid utilization. It is specific for the M and S phases of the cell cycle.

PHARMACOKINETICS

Oral Absorption

bioavailability: 26-45%

Distribution

spleen, liver, kidneys, lungs, thymus;
 heart, muscles, minimal in fat, brain,
 bone marrow, rapid uptake and
 extensive distribution in lung cells is up
 to 300-fold more concentrated than in
 serum; enters breast-milk
 cross blood brain barrier? No information
 Vd- 24 4-40 L/Kg

PPB- highly bound to platelets (98.3%),
 lymphocytes, α -acid-glycoproteins,
 albumin and lipoproteins (79.6-91.2%)

Metabolism

hepatic; two metabolites- vinorelbine-N-
 oxide, deacetylvinorelbine
 metabolite(s):
 active- deacetylvinorelbine
 inactive- vinorelbine-N-oxide

Excretion

fecal (46% - 50%), biliary (25.8%), renal
 (18%)
 Urine: 10-12% unchanged; small
 amounts of deacetylvinorelbine
 $t_{1/2}$ - oral: 24-56 hours; I.V.: 42-45 hours
 Cl- 0.97-1.26L/hr/Kg

ANTIEMETIC RISK

LOW RISK (Less than 10% of patients)
 • No routine antiemetic pre-
 chemotherapy or post-chemotherapy

See Nausea & Vomiting Guidelines for more detail

IV COMPATIBILITY

sodium chloride 0.9% or 0.45%
 dextrose 5% Ringer's or lactated
 Ringer's solution

ROUTES

intravenous injection into free-flowing IV
 infusion or large central vein (6-
 10 minutes)
 Rapid direct injection over 1-2 minutes
 intravenous infusion
 over 20-60 minutes in peripheral vein
 intramuscular, subcutaneous, intrathecal
 -not recommended

ADMINISTRATION

- Push through sidearm of free flowing IV (5% Dextrose, Normal Saline); Inject over 6-10 minutes. Flush with at least 75-125mL of IV solution (*administering nurse should be certified to administer IV push chemotherapy agents*)
- May add to 50mL minibag (5% Dextrose, Normal Saline) to a final concentration 0.5-2mg/mL; Infuse over 6-10 minutes through free-flowing IV
- If extravasation occurs during administration, discontinue immediately and infuse the remaining dose through another IV site (into another vein)
- Protect from light

EXTRAVASATION HAZARD

injection site reactions common
 (redness, increased warmth, pain,
 discolouration of vein)
 Follow Extravasation Guidelines

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic** type are common

IMMEDIATE ONSET (hours to days)

* **myelosuppression**, increased

susceptibility to infection

nausea, vomiting (44%)

injection site reaction (28%)

* pulmonary toxicity (acute shortness of breath, bronchospasm)

EARLY ONSET (days to weeks)

anemia (83%)

pulmonary reactions

alopecia (12%)

jaw pain

stomatitis, constipation (35%)

asthenia

CLINICAL MONITORING

RECOMMENDED CRITERIA

• **Complete blood count including differential, platelets and hemoglobin (CBC) and serum uric acid levels** before each cycle of treatment

• Watch for symptoms of **fever or infection**

• **Neurologic toxicity** ratings (Sensory, Constipation) at each visit

SENSORY

0 No change

1. Mild paraesthesia, no deep tendon reflex

2 Mild/moderate sensory loss, moderate paraesthesia

3 Sensory loss interferes with function

CONSTIPATION

0 No change

1 Mild

2 Moderate

3 Severe

4 Ileus >96 hours

Rated At Each Clinic Visit

SUGGESTED CRITERIA

• Baseline and periodic **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]

• Local Site Toxicity ratings, if incident of phlebitis

LOCAL SITE TOXICITY*

0 None

1 Pain

2 Pain & inflammation; phlebitis

3 Ulceration

4 Plastic surgery

Upon Patient Complaint Or Clinical Event

INDICATIONS AND OTHER USES

• Breast cancer

• Lung cancer, non-small cell

OTHER ONCOLOGY USES

Cervical cancer

Lung cancer, small cell

Ovarian cancer

CONTRAINDICATIONS

• hypersensitivity to vinorelbine, or other vinca alkaloids

• pregnancy, breast feeding

• tumour cell infiltration of bone marrow

• granulocytopenia, thrombocytopenia

Continued Next Page...

VINORELBINE

DOSING

1 week:

- 30 mg/m² (range 7.5-35 mg/m²) as a single agent or 25 mg/m² in combination with other agents IV for one dose on day 1

2 weeks:

- 25 mg/m² IV for one dose on day 1

3 weeks:

- 30 mg/m² (range 25-30 mg/m²) IV for one dose on days 1 and 8 (total dose per cycle 60 mg/m² [range 50-60 mg/m²])
- 8 mg/m² IV bolus followed by 8-9 mg/m²/day over 24 hours for 4 consecutive days (total dose per cycle 40-44 mg/m²)

4 weeks:

- 25 mg/m² IV on days 1 and 8 (total dose per cycle 50 mg/m²)

Pediatric: No pediatric indications

Other dosing may be indicated

SIGNIFICANT INTERACTIONS

bone marrow depressants
cisplatin, fluorouracil, ifosfamide, mitomycin (increased pulmonary effects), cisplatin (increased myelosuppression, decreased infections), paclitaxel

Cytochrome P450 2D6 Inhibitor

DOSE ADJUSTMENT CRITERIA

Hepatic dysfunction

(Recommended action)

1. If Bili= 36-50 µmol/L or AST= 60-180 IU/L, REDUCE to **50%** dose
2. If Bili > 50 µmol/L or AST > 180 IU/L, REDUCE to **25%** dose

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-
Intermediate Level, indication
restrictions

CDHA Status Formulary- Restricted
Non-small cell lung cancer, metastatic
breast cancer

Pharmacare Status Formulary (red)

Continued Next Page...

VINORELBINE

PHARMACEUTICAL CONSIDERATIONS

For intravenous use only: Intrathecal administration of other vinca alkaloids has resulted in death. Syringes containing this product should be labeled:

"WARNING – FATAL IF GIVEN INTRATHECALLY"

Injection:

10 mg, 50 mg vials, each mL contains 10 mg vinorelbine, preservative-free, discard unused portion. Store in the refrigerator, in the original package to protect from light. Avoid freezing. Vinorelbine is initially clear and colourless to pale yellow, but may develop a slightly darker yellow to light amber colour in time. This does not indicate a change which should preclude its use. 3 Unopened vials are stable for up to 72 hours at room temperature.

Diluted solution for infusion:

For direct IV injection, dilute with D5W or NS to 1.5-3 mg/mL. Stable for up to 24 hours when stored in polypropylene syringes at room temperature under normal ambient light. For intermittent infusion, dilute with D5W, NS, 1/2 NS, D5 1/2 NS, Ringer's solution or lactated Ringer's solution to 0.5-2 mg/mL. Stable for up to 24 hours when stored in polyvinylchloride bags at room temperature under normal ambient light.

Bacterial challenge:

Vinorelbine 0.1 mg/mL diluted in NS and stored at 22°C did not exhibit an antimicrobial effect on the growth of four organisms inoculated into the solution. Diluted solutions should be stored under refrigeration whenever possible and the potential for microbiological growth be considered when assigning expiration periods.

Compatibility:

Compatible with potassium chloride. The following are compatible via Y-site injection: bleomycin, calcium gluconate, carboplatin, carmustine, cisplatin, cyclophosphamide, cytarabine, dacarbazine, dactinomycin, daunorubicin, dexamethasone, diphenhydramine, doxorubicin, doxorubicin liposomal, droperidol, etoposide, fludarabine, gemcitabine, granisetron, heparin, hydrocortisone, hydromorphone, idarubicin, ifosfamide, lorazepam, mechlorethamine, melphalan, meperidine, methotrexate, metoclopramide, mitoxantrone, morphine, ondansetron, plicamycin, streptozocin, teniposide, vinblastine and vincristine.

Incompatibility:

The following are incompatible via Y-site injection: fluorouracil, methylprednisolone, mitomycin, sodium bicarbonate and thiotepea.

ZOLEDRONIC ACID

(Biphosphonate: Calcium-Lowering Agents)

Revision Date: Jul 04

COMMERCIAL PRODUCT DESCRIPTION

Brand Name: Zometa® Vials with 4mg for reconstitution with sterile water for injection

MECHANISM OF ACTION

Inhibits osteoclastic bone resorption; zoledronic acid accumulates in bone, where it blocks resorption of mineralized bone & cartilage, inhibits osteoclastic activity (especially osteoclastic hyperactivity and accelerated bone resorption stimulated by tumour). Does not adversely affect formation, mineralization or mechanical properties of normal bone. Zoledronic acid also has direct antitumour activities on some cancer cells, by inhibiting proliferation, inducing apoptosis and inhibiting tumour cell invasion through extracellular matrix. Antitumour effect may be potentiated by other antineoplastic agents.

PHARMACOKINETICS

Oral Absorption

No information

Distribution

No information, 100 times more potent than pamidronate
cross blood brain barrier? No information
Vd - No information PPB - 56%

AUC vs. time curve- linear relationship to dose

Metabolism

No information

Excretion

Triphasic elimination
Rapid decrease at end of infusion to <1% of Cmax after 24 hours
 $t_{1/2} \alpha$ - 0.24 hours, $t_{1/2} \beta$ - 1.87 hours,
 $t_{1/2} \gamma$ - 146 hours

IV COMPATIBILITY

sodium chloride 0.9%
dextrose 5%
Should not be mixed with calcium-containing intravenous infusions.

ROUTES

IV Infusion

ADMINISTRATION

- Mix in 100mL minibag (5% Dextrose, Normal Saline); Infuse over 15 minutes

EXTRAVASATION HAZARD

no reports in literature

DOSING

Intravenous:

- 4 mg (or 8 mg for retreatment) IV for one dose over 15 minutes.
- Retreatment may occur after 7 days if full response is not obtained
- Contraindicated in patients with clinically significant hypersensitivity to other bisphosphonates

Other dosing may be indicated

CONTRAINDICATIONS

- Zoledronic acid is contraindicated in patients with clinically significant hypersensitivity to other bisphosphonates

SIGNIFICANT INTERACTIONS

none reported

INDICATIONS AND OTHER USES

- Treatment of tumour-induced hypercalcemia
- Treatment of bone metastases from solid tumours (prostate cancer, breast cancer, lung cancer, renal cell carcinoma) and osteolytic lesions from multiple myeloma

OTHER ONCOLOGY USES

Prevention of skeletal-related events with prostate cancer

GUIDELINES

Visit the **Cancer Care Nova Scotia** website (www.cancercare.ns.ca) for the guideline on Zoledronic Acid for tumour-induced hypercalcemia

Continued Next Page...

SIDE EFFECTS

* may be life-threatening

side effects in **bold, italic type** are common

IMMEDIATE ONSET

fever (30%), flu-like syndrome
nausea and vomiting
infusion site reactions

EARLY ONSET (days to weeks)

rare: hypocalcemia, hypophosphatemia,
hypomagnesemia
rash, pruritis and chest pain (rare)
bone pain
renal failure

CLINICAL MONITORING

The risk of adverse reactions may be greater in patients with impaired renal function

RECOMMENDED CRITERIA

- Serum electrolytes, including calcium

HYPOCALCEMIA

- 0 Serum Calcium >2.10 mmol/L
- 1 Serum Calcium =2.10 to 1.93 mmol/L
- 2 Serum Calcium =1.92 to 1.74 mmol/L
- 3 Serum Calcium =1.73 to 1.51 mmol/L
- 4 Serum Calcium <1.50 mmol/L

Rated on assessment of anti-hypercalcemia response and at periodic visits or in response to patient complaint

SUGGESTED CRITERIA

- Periodic renal function tests [serum creatinine, electrolytes & BUN], on repeat doses

- Complete blood count including differential, platelets and hemoglobin (CBC), especially if fever

" HYPERCALCEMIA- Response Criteria

- 0 Serum Calcium <2.64 mmol/L
- 1 Serum Calcium =2.64 to 2.88 mmol/L
- 2 Serum Calcium =2.89 to 3.12 mmol/L
- 3 Serum Calcium =3.13 to 3.37 mmol/L
- 4 Serum Calcium >3.37 mmol/L

Rated on assessment of anti-hypercalcemia response and at periodic visits or in response to patient complaint

ADMINISTRATIVE INFORMATION

CCNS Provincial Formulary Status-

Basic Level. Indication restriction-

Provincial Cancer Drug Formulary

CDHA Status Formulary- Restricted

Pharmacare Status Non-Formulary

PHARMACEUTICAL CONSIDERATIONS

Injection

4 mg vials of sterile powder for reconstitution. Store vials at room temperature.

Reconstituted solution for injection

To each vial, add 5 mL SWFI for reconstitution. Reconstituted solution of 4 mg/5 mL may be stored in refrigerator at 2-8 °C for up to 24 hours.

Diluted solution for infusion

Add one or two vials (4 mg or 8 mg doses) to 50 mL Normal Saline. Infuse diluted solution IV over 15 minutes.

Compatibility

IV containers and lines containing glass, polyvinyl chloride (PVC), polyethylene, or polypropylene. Solutions of Normal Saline or 5% Dextrose.

Incompatibility

Any calcium-containing solutions, such as Lactated Ringer's solution. Do not mix with any other drugs. Flush IV lines thoroughly before and after zoledronic acid infusion.

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NOTE: Regimen names in italics are
not in this pocketbook version- See
full version for regimen monograph

BR-ANASTRO

BR

Anastrozole Therapy

(Advanced Breast Cancer)

(Arimidex is the Brand Name for Anastrozole)

Take-Home Prescription-
Unrestricted

ANASTROZOLE 1mg PO daily

(Outpatient prescription in multiples of 1mg tablets)

CONTINUOUS TREATMENT

SUPPORTIVE CARE

ANTIEMETIC REGIMEN

NONE

NOTE

- Prescription costs covered by most third party prescription plans, including Pharmacare
- Anastrozole should only be used in post-menopausal women with advanced breast cancer.

BR-CAPECIT

Capecitabine Therapy

(Advanced Breast Cancer)

(Xeloda™ is the Brand Name for
Capecitabine)

Take-Home Prescription-
Special Authorization Required

CAPECITABINE 1000-1250mg/m² PO BID for 14 days

(Outpatient prescription in multiples of 150mg & 500mg tablets)

- Take capsules WITH FOOD; may divide dose into 3 or 4 divided doses if poorly tolerated
- Prophylaxis To Prevent Hand-Foot Skin Reaction:
 1. Take Pyridoxine (Vitamin B6) 100mg BID or 50mg TID continuously
 2. Apply a hydrating lotion or cream (e.g. Bag Balm, Udder Cream) to hands & feet once or twice daily

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- May give Prochlorperazine 10mg
PO(and/or PR) q4-6h PRN

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Clinical assessment of stomatitis: oral examination upon patient complaint of a sore mouth
- Skin assessment, especially extremities
- Routine assessment of Diarrhea at each clinic visit and telephone reinforcement

DIARRHEA

0 None

1. Increase of 2-3 stools/day over pretreatment
2. Increase of 4-6 stools/day or nocturnal stools
3. Increase of 7-9 stools/day, incontinence, malabsorption
4. Increase of ≥ 10 stools/day, grossly bloody diarrhea, need for parenteral nutrition support

HAND-FOOT SKIN REACTION

0 None

1. Skin changes or dermatitis without pain
2. Skin changes with pain, not interfering with function
3. Skin changes with pain, interfering with function
4. ———

Rated at each clinic visit

BR-CAPECIT

BR

DOSE MODIFICATION

Gastrointestinal or Skin Toxicities

- If any Toxicity Score = Grade 2,
HOLD Capecitabine until score = 0 or 1, resume at 100% dose (if second occurrence, resume at 75% dose, third occurrence at 50%, if fourth occurrence **STOP** Capecitabine)
- If any Toxicity Score = Grade 3,
HOLD Capecitabine until score = 0 or 1, resume at 75% dose or 1000mg/m² BID (if second occurrence, resume at 50% if third occurrence **STOP** Capecitabine)
- If any Toxicity Score = Grade 4,
STOP Capecitabine
If needed, Pharmacy can assist in calculation for dosage reductions

NOTE

- Prescription costs covered by most third party prescription plans
- Pharmacare patients will require a physician letter, requesting approval for coverage*
- The cost per treatment course (i.e. 14 days) can range from \$700-1,100, depending upon patient

GUIDELINE

See the CCNS Website
www.cancercare.ns.ca for the guideline on Capecitabine for Breast cancer

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

DOISING CALCULATION TABLE (1250mg/m² dose)

BSA	≤1.24	1.25	1.37	1.52	1.65	1.77	1.92	2.05	≥2.18
		-1.36	-1.51	-1.64	-1.76	-1.91	-2.04	-2.17	
Daily Dose	3000 mg	3300 mg	3600 mg	4000 mg	4300 mg	4600 mg	5000 mg	5300 mg	5600 mg
				<u>Tablets per dose</u>					
150mg	0	1	2	0	1	2	0	1	2
500mg	3	3	3	4	4	4	5	5	5

DOISING CALCULATION TABLE (1000mg/m² dose)

BSA	≤1.22	1.23	1.40	1.58	1.73	1.90	2.08	2.23	≥2.40
		-1.39	-1.57	-1.72	-1.89	-2.07	-2.22	-2.39	
Daily Dose	2300 mg	2600 mg	3000 mg	3300 mg	3600 mg	4000 mg	4300 mg	4600 mg	5000 mg
				<u>Tablets per dose</u>					
150mg	1	2	0	1	2	0	1	2	0
500mg	2	2	3	3	3	4	4	4	5

BR-CEF*PO

BR

Cyclophosphamide PO- Epirubicin- Fluorouracil Chemotherapy

(Breast Cancer- Adjuvant
treatment of early stage, Locally
Advanced or Inflammatory

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

EPIRUBICIN 60mg/m² IV Day 1 & Day 8 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV over at least 3-5 minutes
- Slow down injection rate if erythematous streaking occurs

5-FLUOROURACIL 500mg/m² IV Day 1 & Day 8 (Round to nearest 25mg)

- Slow push through sidearm of free flowing IV

CYCLOPHOSPHAMIDE 75mg/m² PO qAM x 14 days- Start on Day 1 (Outpatient prescription in multiples of 25mg tablets)

REPEAT EVERY 28 DAYS For a Usual Total of 6 Cycles

Antibiotic Prophylaxis

CO-TRIMOXAZOLE DS 1 tablet PO BID

(OR: CIPROFLOXACIN 500mg PO BID)

- Continuous administration for 6 months OR
- Days 10-24 each treatment cycle (outpatient perscription)

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses. **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days. or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *When available in Canada*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)

Continued Next Page...

BR-CEF*PO

BR

CLINICAL MONITORING

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Clinical assessment of stomatitis**, oral examination upon patient complaint of a sore mouth
- **Baseline renal function tests** (if failure suspected) [serum creatinine, electrolytes & BUN]
- **Baseline liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]
- Clinical exam for symptoms of **Congestive Heart Failure**; Baseline and Periodic **cardiac tests** [Echocardiograms, WMS studies and/or all Angiogram scans] for all patients with cardiac risk factors or patients at or above the threshold dose levels

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < $1.5 \times 10^9/L$, or if Platelets < $100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Renal failure (*Suggested action*)

1. If Creatinine Clearance < 12 ml/min, **OMIT** all drugs

Hepatic dysfunction

1. If Bili = $26-51 \mu\text{mol/L}$ or AST = 60-180 IU/L, give **50%** of Epirubicin dose
2. If Bili = $52-85 \mu\text{mol/L}$ or AST > 180 IU/L, give **25%** of Epirubicin dose
3. If Bili > $85 \mu\text{mol/L}$, **OMIT** all drugs (*Suggested action*)

NOTE

- Prophylactic Ciprofloxacin is substituted for Co-trimoxazole in patients with *known allergy to sulfa antibiotics*.

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT
Approx. 45 minutes

BR-CMF*IV

Cyclophosphamide IV- Methotrexate- Fluorouracil Chemotherapy (Advanced Breast Cancer)

BASIC LEVEL REGIMEN-
Community Hospital with Oncology
Nurses

METHOTREXATE 40mg/m² IV Day 1 (Round to nearest 5mg)

- Slow push through sidearm of free flowing IV

5-FLUOROURACIL 600mg/m² IV Day 1 (Round to nearest 25mg)

- Slow push through sidearm of free flowing IV

CYCLOPHOSPHAMIDE 600mg/m² IV Day 1 (Round to nearest 10mg)

- Mix in 250mL bag (5% Dextrose, Normal Saline); Infuse over 60 minutes

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

Pre-Chemotherapy-

- Dopamine Receptor Antagonist PO (Prochlorperazine 10mg PO or Metoclopramide 10mg PO), **AND**
- Dexamethasone 8mg PO

Post-Chemotherapy-

- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10 mg PO q4h PRN)
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth
- Urinalysis (RBCs)- ONLY in response to patient complaint
- Baseline and periodic liver function tests [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]
- Serum creatinine levels before each cycles

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Renal failure (Suggested action)

1. If Creatinine Clearance = 12-18mL/min or Serum Creatinine= 100-180µmol/L, give **50%** dose
2. If Creatinine Clearance < 12mL/min or Serum Creatinine > 180µmol/L, **OMIT** dose

Hepatic dysfunction (Suggested action)

1. If Bili = 50-85µmol/L or AST > 180IU/L, give **50%** dose
2. If Bili > 85µmol/L, **OMIT** dose

NOTE

CMF*PO is usually recommended instead of CMF*IV, unless the patient cannot tolerate oral Cyclophosphamide.

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:
Approx. 1 hour

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

[Rev 11/01]

BR-CMF*PO

Cyclophosphamide PO- Methotrexate- Fluorouracil Chemotherapy

(Breast Cancer - Adjuvant or Advanced
Treatment)

BASIC LEVEL REGIMEN-
Community Hospital with Oncology
Nurses

BR

METHOTREXATE 40mg/m² IV Day 1 & Day 8 (Round to nearest 5mg)

- Inject by direct IV push, followed by a Normal Saline flush, if no IV line has been set up
- May give by slow push through sidearm of free flowing IV

5-FLUOROURACIL 600mg/m² IV Day 1 & Day 8 (Round to nearest 25mg)

- Inject by direct IV push, followed by a Normal Saline flush, if no IV line has been set up
- May give by slow push through sidearm of free flowing IV

CYCLOPHOSPHAMIDE 100mg/m² PO daily for 14 days- Start on Day 1

(Outpatient prescription in multiples of 25mg tablets)

REPEAT EVERY 28 DAYS

For a Usual Total of 6 Cycles if Adjuvant Treatment

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

Pre-Chemotherapy-

- Dopamine Receptor Antagonist PO
(Prochlorperazine 10mg PO or
Metoclopramide 10mg PO)

Post-Chemotherapy-

- Dopamine Receptor Antagonist PRN
(Prochlorperazine 10mg PO q4-6h
PRN, or Metoclopramide 10 mg PO
q4h PRN)
- Oral hydration is strongly encouraged.
poorly hydrated patients may need
more IV hydration

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets
< 100 x 10⁹/L, notify physician and
HOLD dose for 1 week

Renal failure (Suggested action)

1. If Creatinine Clearance = 12-18mL/min
or Serum Creatinine = 100-180µmol/L,
give **50%** dose
2. If Creatinine Clearance < 12mL/min or
Serum Creatinine > 180µmol/L, **OMIT**
dose

Hepatic dysfunction (Suggested action)

1. If Bili = 50-85µmol/L or AST > 180IU/L,
give **50%** dose
2. If Bili > 85µmol/L, **OMIT** dose

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:

Approx. 30 minutes

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Clinical assessment of stomatitis, oral examination upon patient complaint of sore mouth
- Urinalysis (RBCs)- ONLY in response to patient complaint
- Baseline and periodic liver function tests [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]
- Serum creatinine levels before each cycles

[Rev 11/01]

BR-DOCETAX

Docetaxel Chemotherapy

(Advanced Breast Cancer)

INTERMEDIATE LEVEL REGIMEN-

Regional Hospital with Dedicated
Cancer Treatment Unit

PREMEDICATIONS:

DEXAMETHASONE 8mg PO, 3 doses before chemotherapy (evening before, morning of and 1 hour before chemotherapy), then 8mg PO BID for 3 doses after chemotherapy

DOCETAXEL 100mg/m² IV Day 1 (Round to nearest 3mg)

- Mix in 250mL bag (5% Dextrose or Normal Saline) to a maximum concentration of 1.0-0.3mg/mL; Use non-PVC tubing; Infuse through main IV line over 1 hour

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

INTERMEDIATE RISK

Pre-Chemotherapy-

- Dopamine Receptor Antagonist PO (Prochlorperazine 10mg PO, or Metoclopramide 10mg PO)

Post-Chemotherapy-

- Dopamine Receptor Antagonist PRN ((Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10mg PO q4h PRN)

DEXAMETHASONE Alternate Pre- & Postmedication Regimens:

- May give 20mg PO 12hr & 6hr before chemotherapy, then 8mg PO bid for 4 days after chemotherapy
- May give 8mg PO at 13hr, 7hr & 1hr before chemotherapy, then 8mg PO bid for 3 days after chemotherapy

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Hepatic dysfunction

1. If AST or ALT > 60 IU/L (> 1.5X ULN) or if Alk Phos > 300 IU/L (> 2.5X ULN), reduce Docetaxel to **75% dose**
2. If AST or ALT > 200 IU/L (> 5X ULN) or if Alk Phos > 600 IU/L (> 5X ULN), **HOLD** Docetaxel dose and contact physician

ALTERNATE ADJUSTMENT:

3. If LFTs > 1.5x ULN or Bilirubin > ULN (> 26µmol/L) during treatment, **HOLD** Docetaxel dose for 3 weeks and re-test
ULN = upper limit of normal for lab value
(Recommended action)

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

BR-DOCETAX

BR

CLINICAL MONITORING

- **Complete blood count** including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- **Baseline liver function tests** (if liver failure suspected) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]
- Watch for symptoms of **fever or infection**
- **Clinical assessment of stomatitis**, oral examination upon patient complaint of a sore mouth
- **Skin assessment** at each visit, including nails and infusion veins
- Monitor **fluid retention** at each visit

SKIN TOXICITY

- 0 None
- 1 Hyperpigmentation
- 2 Atrophy
- 3 Subcutaneous fibrosis
- 4 Desquamation, ulceration, or necrosis

NAIL CHANGES

- 0 Normal
- 1 Discolouration or ridging (Vailonychia) or pitting
- 2 Partial or complete loss of nail(s) or pain in nailbeds
- 3 -
- 4 -

FLUID RETENTION

- 0 None
- 1 Mild peripheral edema
- 2 Pleural edema, outpatient management
- 3 Pleural edema, inpatient management
- 4 Intubation required

Rated at each clinic visit

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:

Approximately 2 hours

Weekly Docetaxel Chemotherapy

(Advanced Breast Cancer)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

PREMEDICATIONS:

DEXAMETHASONE 4mg PO, 3 doses before chemotherapy (evening before, morning of and 1 hour before chemotherapy)

DOCETAXEL 30-35mg/m² IV Day 1 (Round to nearest 3mg)

- Mix in 250mL bag (5% Dextrose or Normal Saline) to a maximum concentration of 1.0-0.3mg/mL; Use non-PVC tubing; Infuse through main IV line over 1 hour

REPEAT EVERY 7 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

INTERMEDIATE RISK

Pre-Chemotherapy-

- Dopamine Receptor Antagonist PO (Prochlorperazine 10mg PO, or Metoclopramide 10mg PO)

Post-Chemotherapy-

- Dopamine Receptor Antagonist PRN ((Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10mgPO q4h PRN)

DEXAMETHASONE Alternate Pre- & Postmedication Regimens:

- May give 20mg PO 12hr & 6hr before chemotherapy, then 8mg PO bid for 4 days after chemotherapy
- May give 8mg PO at 13hr, 7hr & 1hr before chemotherapy, then 8mg PO bid for 3 days after chemotherapy

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets <100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Hepatic dysfunction

1. If AST or ALT >60IU/L (>1.5X ULN) or if Alk Phos >300IU/L (>2.5X ULN), reduce Docetaxel to **75% dose**
2. If AST or ALT >200IU/L (>5X ULN) or if Alk Phos >600IU/L (>5X ULN), **HOLD** Docetaxel dose and contact physician

ALTERNATE ADJUSTMENT

3. If LFTs > 1.5x ULN or Bilirubin >ULN (>26µmol/L) during treatment, **HOLD** Docetaxel dose for 3 weeks and re-test
ULN = upper limit of normal for lab value (Recommended action)

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

CLINICAL MONITORING

- **Complete blood count** including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- **Baseline liver function tests** (if liver failure suspected) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]
- Watch for symptoms of **fever or infection**
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Skin assessment** at each visit, including nails and infusion veins
- Monitor **fluid retention** at each visit

SKIN TOXICITY

- 0. None
- 1. Hyperpigmentation
- 2. Atrophy
- 3. Subcutaneous fibrosis
- 4. Desquamation, ulceration, or necrosis

NAIL CHANGES

- 0. Normal
- 1. Discolouration or ridging (Vailonychia) or pitting
- 2. Partial or complete loss of nail(s) or pain in nailbeds
- 3. -
- 4. -

FLUID RETENTION

- 0. None
- 1. Mild peripheral edema
- 2. Pleural edema, outpatient management
- 3. Pleural edema, inpatient management
- 4. Intubation required

Rated at each clinic visit

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:

Approximately 2 hours

BR-DDC

Docetaxel-Doxorubicin- Cyclophosphamide (TAC) Chemotherapy

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

(Adjuvant Treatment Breast Cancer- Node positive & high-risk node negative)

PREMEDICATIONS:

DEXAMETHASONE 8mg PO, 3 doses before chemotherapy (evening before, morning of and 1 hour before chemotherapy), then 8mg PO BID for 3 doses after chemotherapy

DOCETAXEL 100mg/m² IV Day 1 (Round to nearest 3mg)

- Mix in 250mL bag (5% Dextrose or Normal Saline) to a maximum concentration of 1.0-0.3mg/mL; Use non-PVC tubing; Infuse through main IV line over 1 hour

DOXORUBICIN 50mg/m² IV Day 1 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV over at least 3-5 minutes
- Slow down injection rate if erythematous streaking occurs

CYCLOPHOSPHAMIDE 500mg/m² IV Day 1 (Round to nearest 10mg)

- Mix in 250mL bag (5% Dextrose or Normal Saline); Infuse over 60 minutes

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *When available in Canada*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration
- Inadequate total hydration may result in dose-related hemorrhagic cystitis

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

Continued Next Page...

BR-DDC

BR

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Hepatic dysfunction (Docetaxel) (Recommended action)

1. If AST or ALT $> 60 IU/L$ ($> 1.5 \times ULN$) or if Alk Phos $> 300 IU/L$ ($> 2.5 \times ULN$), reduce Docetaxel to **75% dose**
2. If AST or ALT $> 200 IU/L$ ($> 5 \times ULN$) or if Alk Phos $> 600 IU/L$ ($> 5 \times ULN$), **HOLD** Docetaxel dose and contact physician

ALTERNATE ADJUSTMENT

3. If LFTs $> 1.5 \times ULN$ or Bilirubin $> ULN$ ($> 26 \mu mol/L$) during treatment, **HOLD** Docetaxel dose for 3 weeks and re-test

ULN = upper limit of normal for lab value

Hepatic dysfunction (Doxorubicin) (Suggested action)

1. If Bili = $26-51 \mu mol/L$ or AST = $60-180 IU/L$, give **50%** of Doxorubicin dose
2. If Bili = $52-85 \mu mol/L$ or AST $> 180 IU/L$, give **25%** of Doxorubicin dose
3. If Bili $> 85 \mu mol/L$, **OMIT** Doxorubicin dose

Renal failure

1. If Creatinine Clearance $< 18 mL/min$ or Serum Creatinine $> 265 \mu mol/L$, reduce Doxorubicin & Cyclophosphamide to **50% dose**

CLINICAL MONITORING

- **Complete blood count** including differential, platelets and **hemoglobin (CBC)** before each cycle of treatment
- **Urinalysis (RBCs)**- routine for high intravenous doses; periodic for low IV dose/and in response to patient complaint
- Baseline **renal function tests** (before each cycle of chemotherapy) [serum creatinine, electrolytes & BUN]
- Baseline **liver function tests** (before each cycle of chemotherapy) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]
- Watch for symptoms of **fever or infection**
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Skin assessment** at each visit, including nails and infusion veins
- Monitor **fluid retention** at each visit
- Clinical exam for symptoms of **Congestive Heart Failure**
- Baseline and periodic **cardiac tests** [Echocardiograms, WMS studies, and/or all angiography scans] for all patients with cardiac risk factors or patients at or above the threshold dose levels

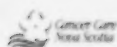
NOTE

Although there have been promising early results, the addition of Docetaxel to Doxo-Cyclo has not been conclusively proven superior to Doxo-Cyclo alone, and it is not recommended for routine use (due to increased cost and patient toxicity without improved overall survival)

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT
Approximately 3 hours

[Rev 12/04]

**Docetaxel-Capecitabine
Chemotherapy***(Advanced Breast Cancer)***BR-DOCE-CAPE****INTERMEDIATE LEVEL REGIMEN-**
Regional Hospital with Dedicated
Cancer Treatment Unit**Take-Home Prescription
(Capecitabine)- Special
Authorization Required****PREMEDICATIONS:**

DEXAMETHASONE 8mg PO, 3 doses before chemotherapy (evening before, morning of and 1 hour before chemotherapy), then 8mg PO BID for 3 doses after chemotherapy

DOCETAXEL 75mg/m² IV Day 1 (Round to nearest 3mg)

- Mix in 250mL bag (5% Dextrose or Normal Saline) to a maximum concentration of 1.0-0.3mg/mL. Use non-PVC tubing. Infuse through main IV line over 1 hour

REPEAT EVERY 21 DAYS

CAPECITABINE 1000-1250mg/m² PO BID for 14 days

(Outpatient prescription in multiples of 150mg & 500mg tablets)

- Take capsules **WITH FOOD**; may divide dose into 3 or 4 divided doses if poorly tolerated
- Prophylaxis To Prevent Hand-Foot Skin Reaction:
 - 1 Take Pyridoxine (Vitamin B6) 100mg BID or 50mg TID continuously
 - 2 Apply a hydrating lotion or cream (e.g. Bag Balm, Udder Cream) to hands & feet once or twice daily

REPEAT EVERY 21 DAYS**SUPPORTIVE CARE****ANTIEMETIC REGIMEN: INTERMEDIATE RISK**Pre-Chemotherapy-

- Dopamine Receptor Antagonist PO (Prochlorperazine 10mg PO, or Metoclopramide 10mg PO)

Post-Chemotherapy-

- Dopamine Receptor Antagonist PRN ((Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10mg PO q4h PRN)

DEXAMETHASONE Alternate Pre- & Postmedication Regimens

- May give 20mg PO 12hr & 6hr before chemotherapy, then 8mg PO bid for 4 days after chemotherapy
- May give 8mg PO at 13hr, 7hr & 1hr before chemotherapy, then 8mg PO bid for 3 days after chemotherapy

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

BR-DOCE-CAPE

BR

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Baseline liver function tests (if liver failure suspected) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]
- Watch for symptoms of fever or infection
- Clinical assessment of stomatitis, oral examination upon patient complaint of a sore mouth
- Skin assessment at each visit, including nails and infusion veins
- Routine assessment of Diarrhea, at each clinic visit and telephone reinforcement
- Monitor fluid retention at each visit

SKIN TOXICITY

- 0 None
- 1 Hyperpigmentation
- 2 Atrophy
- 3 Subcutaneous fibrosis
- 4 Desquamation, ulceration, or necrosis

FLUID RETENTION

- 0 None
- 1 Mild peripheral edema
- 2 Pleural edema, outpatient management
- 3 Pleural edema, inpatient management
- 4 Intubation required

Rated at each clinic visit

DIARRHEA

- 0 None
- 1 Increase of 2-3 stools/day over pretreatment
- 2 Increase of 4-6 stools/day or nocturnal stools
- 3 Increase of 7-9 stools/day, incontinence, malabsorption
- 4 Increase of ≥ 10 stools/day, grossly bloody diarrhea, need for parenteral nutrition support

HAND-FOOT SKIN REACTION

- 0 None
- 1 Skin changes or dermatitis without pain
- 2 Skin changes with pain, not interfering with function
- 3 Skin changes with pain, interfering with function
- 4 —

Rated at each clinic visit

GUIDELINE

See the CCNS Website
www.cancercare.ns.ca for the
guideline on Capecitabine for Breast
cancer

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT
Approximately 2 hours

BR-DOCE-CAPE

DOSE MODIFICATION

Hematologic Toxicities

- 1 If ANC $< 1.5 \times 10^9/L$ or if Platelets $< 100 \times 10^9/L$, notify physician and HOLD dose for 1 week

Hepatic dysfunction (Recommended action)

- 1 If AST or ALT $> 60 IU/L$ ($> 1.5 \times ULN$) or if Alk Phos $> 300 IU/L$ ($> 2.5 \times ULN$), reduce Docetaxel to **75% dose**
- 2 If AST or ALT $> 200 IU/L$ ($> 5 \times ULN$) or if Alk Phos $> 600 IU/L$ ($> 5 \times ULN$), HOLD Docetaxel dose and contact physician

ALTERNATE ADJUSTMENT

- 3 If LFTs $> 1.5 \times ULN$ or Bilirubin $> ULN$ ($> 26 \mu mol/L$) during treatment, HOLD Docetaxel dose for 3 weeks and re-test

ULN = upper limit of normal for lab value

Gastrointestinal or Skin Toxicities

- 1 If any Toxicity Score = Grade 2, **HOLD** Capecitabine until score = 0 or 1, resume at 100% dose (if second occurrence, resume at 75% dose, third occurrence at 50%, if fourth occurrence **STOP** Capecitabine)
- 2 If any Toxicity Score = Grade 3, **HOLD** Capecitabine until score = 0 or 1, resume at 75% dose or 1000mg/m² BID (if second occurrence, resume at 50% if third occurrence **STOP** Capecitabine)
- 3 If any Toxicity Score = Grade 4, **STOP** Capecitabine
If needed, Pharmacy can assist in calculation for dosage reductions

DOSING CALCULATION TABLE (1250mg/m² dose)

BSA	≤ 1.24	1.25	1.37	1.52	1.65	1.77	1.92	2.05	≥ 2.18
		-1.36	-1.51	-1.64	-1.76	-1.91	-2.04	-2.17	
Daily Dose	3000 mg	3300 mg	3600 mg	4000 mg	4300 mg	4600 mg	5000 mg	5300 mg	5600 mg
				Tablets per dose					
150mg	0	1	2	0	1	2	0	1	2
500mg	3	3	3	4	4	4	5	5	5

DOSING CALCULATION TABLE (1000mg/m² dose)

BSA	≤ 1.22	1.23	1.40	1.58	1.73	1.90	2.08	2.23	≥ 2.40
		-1.39	-1.57	-1.72	-1.89	-2.07	-2.22	-2.39	
Daily Dose	2300 mg	2600 mg	3000 mg	3300 mg	3600 mg	4000 mg	4300 mg	4600 mg	5000 mg
				Tablets per dose					
150mg	1	2	0	1	2	0	1	2	0
500mg	2	2	3	3	3	4	4	4	5

BR-DOCE-TRAST

Docetaxel-Trastuzumab Chemotherapy

(Treatment of Advanced Breast Cancer
in Women whose Tumours Overexpress
the HER2 Protein)

First Cycle -
ADVANCED LEVEL REGIMEN-
Provincial Cancer Centre

Other Cycles (if no reaction) -
INTERMEDIATE LEVEL REGI-
MEN- Regional Hospital with
Dedicated Cancer Treatment Unit

BR

PREMEDICATIONS:

May give ACETAMINOPHEN 650mg PO and/or DIPHENHYDRAMINE 50mg PO

TRASTUZUMAB 4mg/Kg Loading Dose Day 1 Only

DO NOT ADMINISTER AS IV PUSH OR BOLUS

- Mix in 250mL solution (Normal Saline, do NOT mix in 5% Dextrose)
- Infuse IV over 90 minutes, then observe for 60 minutes

2mg/Kg Maintenance Dose Weekly from Day 8

- Infuse IV over 30 minutes (longer, if hypersensitivity reaction), then observe for 30 minutes
- Mix in 250mL solution (Normal Saline, do NOT mix in 5% Dextrose)

REPEAT EVERY 7 DAYS - Until Disease Progression

PREMEDICATIONS:

DEXAMETHASONE 8mg PO, 3 doses before chemotherapy (evening before, morning of and 1 hour before chemotherapy), then 8mg PO BID for 3 doses after chemotherapy

DOCETAXEL 100mg/m² IV Day 1 (Round to nearest 3mg)

- Mix in 250mL bag (5% Dextrose or Normal Saline) to a maximum concentration of 1.0-0.3mg/mL; Use non-PVC tubing; Infuse through main IV line over 1 hour

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: INTERMEDIATE RISK

Pre-Chemotherapy-

- Dopamine Receptor Antagonist PO (Prochlorperazine 10mg PO, or Metoclopramide 10mg PO)

Post-Chemotherapy-

- Dopamine Receptor Antagonist PRN ((Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10mg PO q4h PRN)

DEXAMETHASONE Alternate Pre- & Postmedication Regimens:

- May give 20mg PO 12hr & 6hr before chemotherapy, then 8mg PO bid for 4 days after chemotherapy
- May give 8mg PO at 13hr, 7hr & 1hr before chemotherapy, then 8mg PO bid for 3 days after chemotherapy

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

Continued Next Page...

BR-DOCE-TRAST

CLINICAL MONITORING

Docetaxel Criteria

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Baseline liver function tests** (if liver failure suspected) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]
- **Watch for symptoms of fever or infection**
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Skin assessment** at each visit, including nails and infusion veins
- **Monitor fluid retention** at each visit

SKIN TOXICITY

- 0. None
- 1. Hyperpigmentation
- 2. Atrophy
- 3. Subcutaneous fibrosis
- 4. Desquamation, ulceration, or necrosis

NAIL CHANGES

- 0. Normal
- 1. Discolouration or ridging (Villonichia) or pitting
- 2. Partial or complete loss of nail(s) or pain in nailbeds
- 3. -
- 4. -

FLUID RETENTION

- 0. None
- 1. Mild peripheral edema
- 2. Pleural edema, outpatient management
- 3. Pleural edema, inpatient management
- 4. Intubation required

Rated at each clinic visit

Trastuzumab Criteria

- Close observation for infusion-related symptoms, including fever, chills, pain (including pain in tumour), asthenia, and other flu-like symptoms. If treatment is well-tolerated during loading dose and early maintenance doses, observation times may be reduced.
- Baseline and periodic cardiac tests for all patients with cardiac risk factors or suspected cardiac toxicity

CARDIAC

- 0. None
- 1. -
- 2. Asymptomatic, resting ejection fraction decline by >10% baseline, or abnormal cardiac function tests (LVEF >50) with no baseline for comparison
- 3. Mild Congestive Heart Failure, responds to therapy
- 4. Severe/refractory Congestive Heart Failure

BR-DOCE-TRAST

BR

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Hepatic dysfunction

1. If AST or ALT $> 60 IU/L$ ($> 1.5 \times ULN$) or if Alk Phos $> 300 IU/L$ ($> 2.5 \times ULN$), reduce Docetaxel to **75% dose**
 2. If AST or ALT $> 200 IU/L$ ($> 5 \times ULN$) or if Alk Phos $> 600 IU/L$ ($> 5 \times ULN$), **HOLD** Docetaxel dose and contact physician

ALTERNATE ADJUSTMENT

3. If LFTs $> 1.5 \times ULN$ or Bilirubin $> ULN$ ($> 26 \mu mol/L$) during treatment, **HOLD** Docetaxel dose for 3 weeks and re-test
ULN = upper limit of normal for lab value (Recommended action)

GUIDELINE

See the CCNS Website
www.cancercare.ns.ca for the guideline on Trastuzumab for advanced breast cancer

PHYSICIAN'S STANDING ORDERS AVAILABLE FOR THIS REGIMEN

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:

First Cycle- Approx. 5 hours

Other Visits- Approx. 3 hours

DOSING CALCULATION TABLE

Loading Dose & Maintenance Dose in mg/mL (Trastuzumab)

Weight (Kg)	40-45	46-50	51-55	56-60
Loading Dose	170/8.1	189/9.0	210/10.0	231/11.0
Maintenance	84/4.0	94.5/4.5	105/5.0	115.5/5.5
Weight (Kg)	61-65	66-70	71-75	76-80
Loading Dose	250/11.9	271/12.9	290/13.8	311/14.8
Maintenance	126/6.0	134.4/6.4	145/6.9	155.4/7.4
Weight (Kg)	81-85	86-90	91-95	96-100
Loading Dose	330/15.7	351/16.7	370/17.6	391/18.6
Maintenance	166/7.9	174.3/8.3	185/8.8	195.3/9.3
Weight (Kg)	101-105	106-110	111-115	116-120
Loading Dose	409.5/19.5	430.5/20.5	449.4/21.4	470.4/22.4
Maintenance	206/9.8	214.2/10.2	225/10.7	235.2/11.2

BR-DOXO

Doxorubicin Chemotherapy

(Advanced Breast Cancer)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

DOXORUBICIN 60mg/m² IV Day 1 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV over at least 3-5 minutes
- Slow down injection rate if erythematous streaking occurs

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

INTERMEDIATE RISK

Pre-Chemotherapy:

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV). **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)

Post-Chemotherapy:

- Dexamethasone 8 mg PO q24h for 3 doses. **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
- No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
- Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Renal failure

1. If Serum Creatinine > 265µmol/L, reduce Doxorubicin to **50%** dose

Hepatic dysfunction

1. If Bili=26-51µmol/L or AST =60-180IU/L, give **50%** of Doxorubicin dose
2. If Bili= 52-85µmol/L or AST>180IU/L, give **25%** of Doxorubicin dose
3. If Bili>85µmol/L, **OMIT** Doxorubicin dose

(Suggested action)

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

BR-DOXO

BR

CLINICAL MONITORING

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- Clinical exam for symptoms of **Congestive Heart Failure**
- Baseline and periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels [Echocardiograms, WMS studies, and/or all angiography scans]
- Baseline **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]

CARDIAC

0 None

1. —

2 Asymptomatic, resting ejection fraction decline by >10% baseline, or abnormal cardiac function tests (LVEF >50) with no baseline for comparison

3 Mild Congestive Heart Failure, responds to therapy

4 Severe/refractory Congestive Heart Failure

At cumulative dose threshold and subsequent intervals

For Cardiac Toxicity Ratings:

First rating at baseline, then at the cumulative dose **threshold** of **300mg/m²**, & repeat ratings at each cumulative dose **increment** of **100mg/m²** above threshold (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation)

Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given, cardiotoxicity is additive.

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT

Approx. 30 minutes

BR-DOXO*W

Weekly Doxorubicin Chemotherapy

(Advanced Breast Cancer)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

DOXORUBICIN 20-30mg/m² IV Day 1 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV over at least 3-5 minutes
- Slow down injection rate if erythematous streaking occurs

REPEAT EVERY 7 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

INTERMEDIATE RISK

Pre-Chemotherapy:

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)

Post-Chemotherapy:

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
- No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
- Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Renal failure

1. If Serum Creatinine > 265µmol/L, reduce Doxorubicin to **50%** dose

Hepatic dysfunction

1. If Bili=26-51µmol/L or AST =60-180IU/L, give **50%** of Doxorubicin dose
2. If Bili= 52-85µmol/L or AST>180IU/L, give **25%** of Doxorubicin dose
3. If Bili >85µmol/L, **OMIT** Doxorubicin dose
(Suggested action)

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

BR-DOXO*W

BR

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Clinical exam for symptoms of **Congestive Heart Failure**
- Baseline and periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels [Echocardiograms, WMS studies, and/or all angiography scans]
- Baseline **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]

CARDIAC

0 None

1 —

- 2 Asymptomatic, resting ejection fraction decline by >10% baseline; or abnormal cardiac function tests (LVEF >50) with no baseline for comparison
- 3 Mild Congestive Heart Failure, responds to therapy
- 4 Severe/refractory Congestive Heart Failure

At cumulative dose threshold and subsequent intervals

For Cardiac Toxicity Ratings:

First rating at baseline, then at the cumulative dose **threshold** of **300mg/m²**, & repeat ratings at each cumulative dose **increment** of **100mg/m²** above threshold (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation)

Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given, cardiotoxicity is additive.

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:
Approx. 30 minutes

BR-DOXO-CYCLO

Doxorubicin- Cyclophosphamide

(AC) Chemotherapy

(Adjuvant Treatment Breast Cancer)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

DOXORUBICIN 60mg/m² IV Day 1 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV over at least 3-5 minutes
- Slow down injection rate if erythematous streaking occurs

CYCLOPHOSPHAMIDE 600mg/m² IV Day 1 (Round to nearest 10mg)

- Mix in 250mL bag (5% Dextrose or Normal Saline); Infuse over 60 minutes

REPEAT EVERY 21 DAYS For a Usual Total of 4 Cycles

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) **When available in Canada**
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration
- Inadequate total hydration may result in dose-related hemorrhagic cystitis

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Renal failure

1. If Serum Creatinine > 265µmol/L, reduce Doxorubicin to **50%** dose

Hepatic dysfunction (Suggested action)

1. If Bili=26-51µmol/L or AST =60-180IU/L, give **50%** of Doxorubicin dose
2. If Bili= 52-85µmol/L or AST>180IU/L, give **25%** of Doxorubicin dose
3. If Bili >85µmol/L, **OMIT** Doxorubicin dose

Continued Next Page...

BR-DOXO-CYCLO

BR

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- **Urinalysis (RBCs)**- routine for high intravenous doses; periodic for low IV dose/ and in response to patient complaint
- Baseline and routine **renal function tests** (before each cycle of chemotherapy) [serum creatinine, electrolytes & BUN]
- Baseline and routine **liver function tests** (before each cycle of chemotherapy)[serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]
- Clinical exam for symptoms of **Congestive Heart Failure**
- Baseline and periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels [Echocardiograms, WMS studies, and/or all angiography scans]

CARDIAC

0. None

1. —

2. Asymptomatic, resting ejection fraction decline by >10% baseline; or abnormal cardiac function tests (LVEF >50) with no baseline for comparison
3. Mild Congestive Heart Failure, responds to therapy
4. Severe/refractory Congestive Heart Failure

At cumulative dose threshold and subsequent intervals

For Cardiac Toxicity Ratings:

First rating at baseline, then at the cumulative dose **threshold of 300mg/m²**, & repeat ratings at each cumulative dose **increment of 100mg/m²** above threshold (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation)

Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

PATIENT VISIT
CHEMOTHERAPY PATIENT VISIT:
Approx. 90 minutes


BR-DOXO-CYCLO → PACLI

**Doxorubicin-
Cyclophosphamide
(AC) → Paclitaxel**

Chemotherapy

(Adjuvant Treatment Breast Cancer)

**INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit**

DOXORUBICIN 60mg/m² IV Day 1 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV over at least 3-5 minutes
- Slow down injection rate if erythematous streaking occurs

CYCLOPHOSPHAMIDE 600mg/m² IV Day 1 (Round to nearest 10mg)

- Mix in 250mL bag (5% Dextrose or Normal Saline); Infuse over 60 minutes

REPEAT EVERY 21 DAYS For a Usual Total of 4 Cycles

After 4 Cycles of Doxo-Cyclo, Followed by:

PREMEDICATIONS (for Paclitaxel):

DEXAMETHASONE 20mg PO 12 & 6 hours before Paclitaxel

(OR 20mg IV 30 minutes pre Paclitaxel)

DIPHENHYDRAMINE 50mg IV & RANITIDINE 50mg IV

- Admix together in 50mL minibag (Normal Saline); give over 15 minutes, wait 30 minutes before Paclitaxel dose started

PACLITAXEL 175mg/m² IV Day 1 Infuse over 3 hours (Round to nearest 3mg)

- Mix in 500mL bag (5% Dextrose- dilution concentration 0.3-1.2 mg/mL); Use non-PVC equipment, including 0.22 micron in-line filter; Infuse over 3 hours
- Take a baseline blood pressure measurement, if prior hypotension

REPEAT EVERY 21 DAYS For a Usual Total of 4 Cycles

Continued Next Page...

BR-DOXO-CYCLO → PACLI

BR

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: Doxo-Cyclo Cycles- HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *When available in Canada*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)
- Oral hydration is strongly encouraged: poorly hydrated patients may need more IV hydration
- Inadequate total hydration may result in dose-related hemorrhagic cystitis

ANTIEMETIC REGIMEN: Paclitaxel cycles- LOW RISK

- May give Prochlorperazine 10mg PO (or 10mg IV) pre chemo & 10mg PO (or 10mg PR) q4-6h PRN post chemo
- DEXAMETHASONE premedication may be reduced in successive cycles: 12mg PO x 2 doses (cycle 2); 8mg PO x 2 doses (cycle 3); then 4mg PO x 2 doses

ALL CYCLES:

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < $1.5 \times 10^9/L$, or if Platelets < $100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Doxo-Cyclo Cycles:

1. If AST > 70IU/L or Bili > $25\mu\text{mol/L}$, give

Maximum dose of 135mg/m²

Renal failure

1. If Creatinine Clearance < 18mL/min or Serum Creatinine > $265\mu\text{mol/L}$, reduce Doxorubicin & Cyclophosphamide to 50% dose

2. If Bili = $25-50\mu\text{mol/L}$, give **maximum dose of 75mg/m²**

3. If Bili > $50\mu\text{mol/L}$, give **maximum dose of 50mg/m²**

Hepatic dysfunction (Suggested action)

1. If Bili = $26-51\mu\text{mol/L}$ or AST = $60-180\text{IU/L}$, give 50% of Doxorubicin dose
2. If Bili = $52-85\mu\text{mol/L}$ or AST > 180IU/L , give 25% of Doxorubicin dose
3. If Bili > $85\mu\text{mol/L}$, **OMIT** Doxorubicin dose

Paclitaxel Cycles:

Hepatic dysfunction

Continued Next Page...

BR-DOXO-CYCLO → PACLI

CLINICAL MONITORING- Doxo-Cyclo Cycles

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- **Urinalysis (RBCs)**- routine for high intravenous doses; periodic for low IV dose/ and in response to patient complaint
- Baseline and routine **renal function tests** (before each cycle of chemotherapy) [serum creatinine, electrolytes & BUN]
- Baseline and routine **liver function tests** (before each cycle of chemotherapy)[serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]
- Clinical exam for symptoms of **Congestive Heart Failure**
- Baseline and periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels [Echocardiograms, WMS studies, and/or all angiography scans]

CARDIAC

0. None

1. —

2. Asymptomatic, resting ejection fraction decline by >10% baseline; or abnormal cardiac function tests (LVEF >50) with no baseline for comparison

3. Mild Congestive Heart Failure, responds to therapy

4. Severe/refractory Congestive Heart Failure

At cumulative dose threshold and subsequent intervals

For Cardiac Toxicity Ratings:

First rating at baseline, then at the cumulative dose threshold of 300mg/m², & repeat ratings at each cumulative dose increment of 100mg/m² above threshold (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation)

Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

PHYSICIAN'S STANDING ORDERS AVAILABLE FOR THIS REGIMEN

NOTE

Promising early results have failed to result in a significant improvement in overall survival, when the trial of Doxo-Cyclo-->Pacli was compared with Doxo-Cyclo. Therefore, this sequential regimen is not recommended to replace Doxo-Cyclo (due to increased cost and patient toxicity without improved overall survival)

PATIENT VISIT

DOXO-CYCLO CYCLES

Chemotherapy Visit: Approx. 1½ hours

PACLITAXEL CYCLES

Chemotherapy Visit: Approx 5 hours

CLINICAL MONITORING- Pacli Cycles

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Watch for symptoms of fever or infection
- Blood pressure and pulse rate monitoring during drug administration & for the following hour

SENSORY

- 0. No change
- 1. Mild paresthesia, no deep tendon reflex
- 2. Mild/moderate sensory loss, moderate paresthesia
- 3. Sensory loss interferes with function

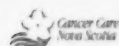
FLU-LIKE SYMPTOMS (*Arthralgia myalgia*)

- 0. None
- 1. Mild
- 2. Moderate
- 3. Severe

HYPERSENSITIVITY

- 0. None
- 1. Transient rash, fever $<38^{\circ}\text{C}$
- 2. Urticaria, fever $\geq 38^{\circ}\text{C}$, bronchospasm
- 3. Serum sickness, bronchospasm, requires parenteral medications
- 4. Anaphylaxis

Rated at each clinic visit

BR-EPIRUB**Epirubicin Chemotherapy**

(Advanced Breast Cancer)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

EPIRUBICIN 35mg IV Days 1, 8 & 15 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV over at least 3-5 minutes
- Slow down injection rate if erythematous streaking occurs

REPEAT EVERY 28 DAYS**SUPPORTIVE CARE****ANTIEMETIC REGIMEN:****INTERMEDIATE RISK**Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV). **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses. **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
- No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
- Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo

DOSE MODIFICATIONHematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$ or if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Renal failure

1. If Serum Creatinine $> 265 \mu\text{mol/L}$, reduce Doxorubicin to **50%** dose

Hepatic dysfunction

1. If Bili = $26-51 \mu\text{mol/L}$ or AST = $60-180 \text{ IU/L}$, give **50%** of Doxorubicin dose
2. If Bili = $52-85 \mu\text{mol/L}$ or AST $> 180 \text{ IU/L}$, give **25%** of Doxorubicin dose
3. If Bili $> 85 \mu\text{mol/L}$, **OMIT** Doxorubicin dose
(Suggested action)

Continued Next Page...

BR-EPIRUB

BR

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Urinalysis (RBCs)- routine for high intravenous doses, periodic for low IV dose/and in response to patient complaint
- Baseline renal function tests (if failure suspected) [serum creatinine, electrolytes & BUN]
- Baseline liver function tests [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]
- Clinical exam for symptoms of Congestive Heart Failure
- Baseline and periodic cardiac tests [Echocardiograms, WMS studies, and/or all angiography scans] for all patients with cardiac risk factors or patients at or above the threshold dose levels

CARDIAC

0. None

1. —

2. Asymptomatic, resting ejection fraction decline by $>10\%$ baseline; or abnormal cardiac function tests (LVEF >50) with no baseline for comparison
3. Mild Congestive Heart Failure, responds to therapy
4. Severe/refractory Congestive Heart Failure

At cumulative dose threshold and subsequent intervals

For Cardiac Toxicity Ratings:

First rating at baseline, then at the cumulative dose threshold of 450mg/m^2 , & repeat ratings at each cumulative dose increment of 150mg/m^2 above threshold (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation)

Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

NOTE

Epirubicin-based regimens for advanced breast cancer are not superior to Doxorubicin-based regimens, but are substantially more expensive. This regimen should only be used in selected patients where drug toxicity differences are important for regimen selection.

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:
Approx. 30 minutes

BR-EXEMEST

Exemestane Therapy

(Advanced Breast Cancer)

(Aromasin® is the Brand Name for Exemestane)

Take-Home Prescription-
Special Authorization Required

EXEMESTANE 25mg PO daily

(Outpatient prescription in multiples of 25mg tablets)

CONTINUOUS TREATMENT

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: NONE

NOTES

- Prescription costs covered by most third party prescription plans
- *Pharmacare patients will require a physician letter, requesting approval for coverage*
- Exemestane should be used in post-menopausal women with advanced breast cancer
- Exemestane may induce a response in women refractory to reversible aromatase inhibitors (eg. Anastrozole, Letrozole)

BR-FAC*IV

Cyclophosphamide IV- Doxorubicin- Fluorouracil (FAC) Chemotherapy

(Advanced Breast Cancer)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

BR

DOXORUBICIN 50mg/m² IV Day 1 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV over at least 3-5 minutes
- Slow down injection rate if erythematous streaking occurs

5-FLUOROURACIL 500mg/m² IV Day 1 & Day 8 (Round to nearest 25mg)

- Slow push through sidearm of free flowing IV
- May be given by direct IV push, followed by a Normal Saline flush, if no IV line has been set up

CYCLOPHOSPHAMIDE 500mg/m² IV Day 1 (Round to nearest 10mg)

- Mix in 100mL bag (5% Dextrose or Normal Saline); Infuse over 30 minutes

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *When available in Canada*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration
- Inadequate total hydration may result in dose-related hemorrhagic cystitis

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BR-FAC*IV

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week then **RESTART** at **20% REDUCED** dose

Renal failure

1. If Creatinine Clearance $< 18\text{mL/min}$ or Serum Creatinine $> 265\mu\text{mol/L}$, reduce Doxorubicin & Cyclophosphamide to **50%** dose

Hepatic dysfunction (Suggested action)

1. If Bili = $26\text{--}51\mu\text{mol/L}$ or AST = $60\text{--}180\text{IU/L}$, give **50%** of Doxorubicin dose
2. If Bili = $52\text{--}85\mu\text{mol/L}$ or AST $> 180\text{IU/L}$, give **25%** of Doxorubicin dose
3. If Bili $> 85\mu\text{mol/L}$, **OMIT** all drugs

CLINICAL MONITORING

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment and on day 10 of first cycle only
- Clinical exam for symptoms of **Congestive Heart Failure**
- Baseline and periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels [Echocardiograms, WMS studies, and/or all angiography scans]
- Baseline **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]
- Baseline **renal function tests** [serum creatinine, electrolytes & BUN]
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Urinalysis (RBCs)**- ONLY in response to patient complaint

CARDIAC

0. None

1. —

2. Asymptomatic, resting ejection fraction decline by $> 10\%$ baseline; or abnormal cardiac function tests (LVEF > 50) with no baseline for comparison
3. Mild Congestive Heart Failure, responds to therapy
4. Severe/refractory Congestive Heart Failure

At cumulative dose threshold and subsequent intervals

For Cardiac Toxicity Ratings:

First rating at baseline, then at the cumulative dose **threshold** of 300mg/m^2 , & repeat ratings at each cumulative dose **increment** of 100mg/m^2 above threshold (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation)

Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:
Day 1 = Approx. 2 hours
Day 8 = Approx. 30 minutes

[Rev 05/02]

BR-FEC*IV

Fluorouracil- Epirubicin- Cyclophosphamide IV Chemotherapy

(Advanced Breast Cancer)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

BR

EPIRUBICIN 75mg/m² IV Day 1 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV over at least 3-5 minutes
- Slow down injection rate if erythematous streaking occurs

5-FLUOROURACIL 500mg/m² IV Day 1 (Round to nearest 25mg)

- Slow push through sidearm of free flowing IV
- May be given by direct IV push, followed by a Normal Saline flush, if no IV line has been set up

CYCLOPHOSPHAMIDE 500mg/m² IV Day 1 (Round to nearest 10mg)

- Mix in 100mL bag (5% Dextrose or Normal Saline); Infuse over 30 minutes

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) **When available in Canada**
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration
- Inadequate total hydration may result in dose-related hemorrhagic cystitis

NOTE

Epirubicin-based regimens for advanced breast cancer are not superior to Doxorubicin-based regimens, but are substantially more expensive. This regimen should only be used in selected patients where drug toxicity differences are important for regimen selection.

Continued Next Page...

BR-FEC*IV

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week then **RESTART** at **20% REDUCED** dose

Renal failure

1. If Creatinine Clearance $< 18 \text{ mL/min}$ or Serum Creatinine $> 265 \mu\text{mol/L}$, reduce Epirubicin & Cyclophosphamide to **50%** dose

Hepatic dysfunction (Suggested action)

1. If Bili = $26\text{--}51 \mu\text{mol/L}$ or AST = $60\text{--}180 \text{ IU/L}$, give **50%** of Epirubicin dose

2. If Bili = $52\text{--}85 \mu\text{mol/L}$ or AST $> 180 \text{ IU/L}$, give **25%** of Epirubicin dose

3. If Bili $> 85 \mu\text{mol/L}$, **OMIT** all drugs

CLINICAL MONITORING

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment and on day 10 of first cycle only
- **Clinical exam** for symptoms of **Congestive Heart Failure**
- **Baseline and periodic cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels [Echocardiograms, WMS studies, and/or all angiography scans]
- **Baseline liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]
- **Baseline renal function tests** [serum creatinine, electrolytes & BUN]
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Urinalysis (RBCs)**- ONLY in response to patient complaint

CARDIAC

0. None

1. —

2. Asymptomatic, resting ejection fraction decline by $> 10\%$ baseline; or abnormal cardiac function tests (LVEF > 50) with no baseline for comparison

3. Mild Congestive Heart Failure, responds to therapy

4. Severe/refractory Congestive Heart Failure

At cumulative dose threshold and subsequent intervals

For Cardiac Toxicity Ratings:

First rating at baseline, then at the cumulative dose **threshold** of **450mg/m²**, & repeat ratings at each cumulative dose **increment** of **150mg/m²** above threshold (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation)

Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:
Approx. 2 hours

[Rev 05/02]

BR-FEC-100*IV

Fluorouracil- Epirubicin 100 mg- Cyclophosphamide IV Chemotherapy

(Adjuvant Treatment- Breast Cancer)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

BR

EPIRUBICIN 100 mg/m² IV Day 1 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV over at least 3-5 minutes
- Slow down injection rate if erythematous streaking occurs

5-FLUOROURACIL 500 mg/m² IV Day 1 (Round to nearest 25mg)

- Slow push through sidearm of free flowing IV
- May be given by direct IV push, followed by a Normal Saline flush, if no IV line has been set up

CYCLOPHOSPHAMIDE 500 mg/m² IV Day 1 (Round to nearest 10mg)

- Mix in 100mL bag (5% Dextrose or Normal Saline); Infuse over 30 minutes

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) **When available in Canada**
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration
- Inadequate total hydration may result in dose-related hemorrhagic cystitis

NOTE

Epirubicin-based regimens for advanced breast cancer are not superior to Doxorubicin-based regimens, but are substantially more expensive. This regimen should only be used in selected patients where drug toxicity differences are important for regimen selection.

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DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week then **RESTART** at **20% REDUCED** dose

Renal failure

1. If Creatinine Clearance $< 18\text{mL/min}$ or Serum Creatinine $> 265\mu\text{mol/L}$, reduce Epirubicin & Cyclophosphamide to **50%** dose

Hepatic dysfunction (Suggested action)

1. If Bili = $26\text{--}51\mu\text{mol/L}$ or AST = $60\text{--}180\text{IU/L}$, give **50%** of Epirubicin dose
2. If Bili = $52\text{--}85\mu\text{mol/L}$ or AST $> 180\text{IU/L}$, give **25%** of Epirubicin dose
3. If Bili $> 85\mu\text{mol/L}$, **OMIT** all drugs

CLINICAL MONITORING

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment and on day 10 of first cycle only
- Clinical exam for symptoms of **Congestive Heart Failure**
- Baseline and periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels [Echocardiograms, WMS studies, and/or all angiography scans]
- Baseline **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]
- Baseline **renal function tests** [serum creatinine, electrolytes & BUN]
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Urinalysis (RBCs)**- ONLY in response to patient complaint

CARDIAC

0. None

1. —

2. Asymptomatic, resting ejection fraction decline by $> 10\%$ baseline; or abnormal cardiac function tests (LVEF > 50) with no baseline for comparison
3. Mild Congestive Heart Failure, responds to therapy
4. Severe/refractory Congestive Heart Failure

At cumulative dose threshold and subsequent intervals

For Cardiac Toxicity Ratings:

First rating at baseline, then at the cumulative dose **threshold** of **450mg/m²**, & repeat ratings at each cumulative dose **increment** of **150mg/m²** above threshold (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation)

Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

PATIENT VISIT
CHEMOTHERAPY PATIENT VISIT:
Approx. 2 hours

BR-LETRO

Letrozole Therapy

(Advanced Breast Cancer)
(Femara® is the Brand Name for
Letrozole)

Take-Home Prescription-
Unrestricted

BR

LETROZOLE 2.5mg PO daily

(Outpatient prescription in multiples of 2.5mg tablets)

CONTINUOUS TREATMENT

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: NONE

NOTES

- Prescription costs covered by most third party prescription plans
- To reduce drug costs, it is advisable to prescribe in lots of 3 months (or longer) once treatment is established. This will reduce cost to the patient or prescription plan
- Letrozole should only be used in post-menopausal women with advanced breast cancer

BR-PACLI

Paclitaxel Chemotherapy

(Advanced Breast Cancer)

INTERMEDIATE LEVEL

REGIMEN- Regional Hospital with
Dedicated Cancer Treatment Unit

BR

PREMEDICATIONS:

DEXAMETHASONE 20mg PO 12 & 6 hours before Paclitaxel

(OR 20mg IV- Infuse over 15 minutes, starting 45 minutes before Paclitaxel)

DIPHENHYDRAMINE 50mg IV & RANITIDINE 50mg IV

- Admix together in 50mL minibag (Normal Saline); give over 15 minutes, wait 30 minutes before Paclitaxel dose started

PACLITAXEL 175mg/m² IV Day 1- Infuse over 3 hours

(Round to nearest 3mg)

- Mix in 500mL bag (5% Dextrose- dilution concentration 0.3-1.2 mg/mL);
Use non-PVC equipment, including 0.22 micron in-line filter; Infuse over 3 hours
- Take a baseline blood pressure measurement, if prior hypotension

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

INTERMEDIATE RISK on Paclitaxel
Treatment Days

Pre-Chemotherapy-

- Serotonin Receptor Antagonist
(Ondansetron 8mg PO- may substitute
Ondansetron 8mg IV, or Granisetron
2mg PO or 1mg IV, or Dolasetron 100-
200mg PO or 100mg IV)

Post-Chemotherapy-

- Serotonin Receptor Antagonist PO
(Ondansetron 8mg PO q12h for 3
doses if given prechemo) **OR**
- No post-chemo serotonin receptor
antagonist if Granisetron or
Dolasetron given pre-chemo **OR**
- Granisetron 2mg PO q24h for 1-2
days, or Dolasetron 100mg PO q24h
for 1-2 days, if given pre-chemo

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management
protocol
- Give Diphenhydramine 50mg IV push &
Hydrocortisone 100mg IV push

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets
< 100 x 10⁹/L, notify physician and
HOLD dose for 1 week

Hepatic dysfunction

1. If AST > 70IU/L or Bili < 25µmol/L,
give **maximum dose of 135mg/m²**
2. If Bili=25-50µmol/L, give **maximum
dose of 75mg/m²**
3. If Bili > 50µmol/L, give **maximum dose
of 50mg/m² (Suggested action)**

BR-PACLI

BR

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Watch for symptoms of **fever or infection**
- Baseline **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]
- **Neurologic** (Sensory) , hypersensitivity and flu-like symptoms toxicity ratings at each visit
- Baseline **blood pressure** and **pulse rate monitoring** during drug administration & for the following hour

SENSORY

- 0. No change
- 1. Mild paresthesia; no deep tendon reflex
- 2. Mild/moderate sensory loss, moderate paresthesia
- 3. Sensory loss interferes with function

FLU-LIKE SYMPTOMS (*Arthralgia myalgia*)

- 0. None
- 1. Mild
- 2. Moderate
- 3. Severe

HYPERSENSITIVITY

- 0. None
- 1. Transient rash; fever $<38^{\circ}\text{C}$
- 2. Urticaria; fever $\geq 38^{\circ}\text{C}$; bronchospasm
- 3. Serum sickness; bronchospasm, requires parenteral medications
- 4. Anaphylaxis

Rated at each clinic visit

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:

Approx. 5 hours

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

BR-PACLI-TRAST

Paclitaxel-Trastuzumab Chemotherapy

(Treatment of Advanced Breast Cancer
in Women whose Tumours Overexpress
the HER2 Protein)

**First Cycle -
INTERMEDIATE LEVEL REGIMEN-**
Regional Hospital with Dedicated
Cancer Treatment Unit

**Other Trastuzumab Cycles (if no
reaction) - BASIC LEVEL
REGIMEN-** Community Hospital
with Oncology Nurses

PREMEDICATIONS:

May give ACETAMINOPHEN 650mg PO and/or DIPHENHYDRAMINE 50mg PO

TRASTUZUMAB 4mg/Kg Loading Dose Day 1 Only

DO NOT ADMINISTER AS IV PUSH OR BOLUS

- Mix in 250mL solution (Normal Saline, do NOT mix in 5% Dextrose)
- Infuse IV over 90 minutes, then observe for 60 minutes

2mg/Kg Maintenance Dose Weekly from Day 8

- Infuse IV over 30 minutes (longer, if hypersensitivity reaction), then observe for 30 minutes
- Mix in 250mL solution (Normal Saline, do NOT mix in 5% Dextrose)

REPEAT EVERY 7 DAYS - Until Disease Progression

PREMEDICATIONS:

DEXAMETHASONE 20mg PO 12 & 6 hours before Paclitaxel

(OR 20mg IV- Infuse over 15 minutes, starting 45 minutes before Paclitaxel)

DIPHENHYDRAMINE 50mg IV & RANITIDINE 50mg IV

- Admix together in 50mL minibag (Normal Saline); give over 15 minutes, wait 30 minutes before Paclitaxel dose started

PACLITAXEL 175mg/m² IV Day 1- Infuse over 3 hours

(Round to nearest 3mg)

- Mix in 500mL bag (5% Dextrose- dilution concentration 0.3-1.2 mg/mL);
Use non-PVC equipment, including 0.22 micron in-line filter; Infuse over 3 hours
- Take a baseline blood pressure measurement, if prior hypotension

REPEAT EVERY 21 DAYS

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BR-PACLI-TRAST

CLINICAL MONITORING

Paclitaxel Criteria

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Watch for symptoms of fever or infection
- Baseline liver function tests [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]
- Neurologic (Sensory) . hypersensitivity and flu-like symptoms toxicity ratings at each visit
- Baseline blood pressure and pulse rate monitoring during drug administration & for the following hour

SENSORY

- 0 No change
- 1 Mild paresthesia; no deep tendon reflex
- 2 Mild/moderate sensory loss, moderate paresthesia
- 3 Sensory loss interferes with function

FLU-LIKE SYMPTOMS (Arthralgia myalgia)

- 0 None
- 1 Mild
- 2 Moderate
- 3 Severe

HYPERSENSITIVITY

- 0 None
- 1 Transient rash; fever $<38^{\circ}\text{C}$
- 2 Urticaria; fever $\geq 38^{\circ}\text{C}$; bronchospasm
- 3 Serum sickness; bronchospasm, requires parenteral medications
- 4 Anaphylaxis

Rated at each clinic visit

Trastuzumab Criteria

- Close observation for infusion-related symptoms, including fever, chills, pain (including pain in tumour), asthenia, and other flu-like symptoms. If treatment is well-tolerated during loading dose and early maintenance doses, observation times may be reduced.
- Baseline and periodic cardiac tests for all patients with cardiac risk factors or suspected cardiac toxicity

CARDIAC

0. None
1. —
2. Asymptomatic, resting ejection fraction decline by $>10\%$ baseline; or abnormal cardiac function tests (LVEF >50) with no baseline for comparison
3. Mild Congestive Heart Failure, responds to therapy
4. Severe/refractory Congestive Heart Failure

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^3/\text{L}$, or if Platelets $< 100 \times 10^3/\text{L}$, notify physician and HOLD Paclitaxel dose for 1 week

Hepatic dysfunction

1. If AST $> 70\text{IU/L}$ or Bili $< 25\mu\text{mol/L}$, give maximum Paclitaxel dose of $135\text{mg}/\text{m}^2$
2. If Bili $= 25\text{--}50\mu\text{mol/L}$, give maximum Paclitaxel dose of $75\text{mg}/\text{m}^2$
3. If Bili $> 50\mu\text{mol/L}$, give maximum Paclitaxel dose of $50\text{mg}/\text{m}^2$ (Suggested action)

BR-PACLI-TRAST

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: INTERMEDIATE RISK on Paclitaxel Treatment Days
Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV)

Post-Chemotherapy-

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

GUIDELINE

See the CCNS Website
www.cancercare.ns.ca for the guideline
on Trastuzumab for advanced breast cancer

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:

First Cycle- Approx. 5 hours

Other Visits- Approx. 3 hours

DOSING CALCULATION TABLE

Loading Dose & Maintenance Dose in mg/mL (Trastuzumab)

Weight (Kg)	40-45	46-50	51-55	56-60
Loading Dose	170/8.1	189/9.0	210/10.0	231/11.0
Maintenance	84/4.0	94.5/4.5	105/5.0	115.5/5.5
Weight (Kg)	61-65	66-70	71-75	76-80
Loading Dose	250/11.9	271/12.9	290/13.8	311/14.8
Maintenance	126/6.0	134.4/6.4	145/6.9	155.4/7.4
Weight (Kg)	81-85	86-90	91-95	96-100
Loading Dose	330/15.7	351/16.7	370/17.6	391/18.6
Maintenance	166/7.9	174.3/8.3	185/8.8	195.3/9.3
Weight (Kg)	101-105	106-110	111-115	116-120
Loading Dose	409.5/19.5	430.5/20.5	449.4/21.4	470.4/22.4
Maintenance	206/9.8	214.2/10.2	225/10.7	235.2/11.2

BR-PAMID

Pamidronate Therapy

(Treatment of Bone Metastases or Bony Pain Associated with Advanced Breast Cancer)

BASIC LEVEL REGIMEN-
Community Hospital with
Oncology Nurses

BR

PAMIDRONATE 90mg IV over 2-4 hours

- Administer concurrently with first-line or salvage cytotoxic chemotherapy
- Mix in 500mL solution (5% Dextrose, Normal Saline) and infuse as outpatient over 2 hours or longer (if observation required)
- Admix into ambulatory pump & infuse over 2-4 hours, or longer, at home for subsequent doses (Intermate pump, other disposable pumps)

REPEAT EVERY 21-28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: NONE

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:
Approximately 4 hours OR 15 minutes
for ambulatory pump

CLINICAL MONITORING

- Serum electrolytes, including calcium, serum creatinine & albumin before each dose.
- If Corrected Serum Calcium* <2.10 μmol/L. **HOLD** dose for 1 week, or until Serum Calcium levels within normal range

HYPOCALCEMIA

0. Serum Calcium >2.10 μmol/L
1. Serum Calcium =2.10 to 1.93 μmol/L
2. Serum Calcium =1.92 to 1.74 μmol/L
3. Serum Calcium =1.73 to 1.51 μmol/L
4. Serum Calcium <1.50 μmol/L

Rated on assessment of anti-hypercalcemia response and at periodic visits or in

response to patient complaint

*Corrected Serum Calcium = Measured
Serum Calcium + [(40 - Serum
Albumin) x 0.02]

BR-TAMOX

Tamoxifen Therapy

(Adjuvant or Advanced Treatment Breast Cancer)

Take-Home Prescription-
Unrestricted

TAMOXIFEN 20mg PO daily

(Outpatient prescription in multiples of 10mg & 20mg tablets)

CONTINUOUS TREATMENT

For a Usual Total of up to 5 Years (If used for Adjuvant Treatment)

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: NONE

CLINICAL MONITORING

- Clinical assessment for gynecological symptoms (endometrial hyperplasia/neoplasia)

NOTES

- Prescription costs covered by all third party prescription plans
- Due to low drug costs, it is advisable to prescribe in lots of 3 months (or longer) once treatment is established. This will reduce cost to the patient or prescription plan.

BR-TRAST

BR

Trastuzumab Chemotherapy

(Treatment of Advanced Breast Cancer in Women whose Tumours Overexpress the HER2 Protein, and Who Have Been Previously Treated with Chemotherapy)

(Herceptin® is the Brand Name for Trastuzumab)

**First Cycle -
INTERMEDIATE LEVEL REGIMEN-**
Regional Hospital with Dedicated
Cancer Treatment Unit

**Other Cycles (if no reaction) -
BASIC LEVEL REGIMEN-**
Community Hospital with
Oncology Nurses

PREMEDICATIONS:

May give ACETAMINOPHEN 650mg PO and/or DIPHENHYDRAMINE 50mg PO

TRASTUZUMAB 4mg/Kg Loading Dose Day 1 Only

DO NOT ADMINISTER AS IV PUSH OR BOLUS

- Mix in 250mL solution (Normal Saline, do **NOT** mix in 5% Dextrose)
- Infuse IV over 90 minutes, then observe for 60 minutes

2mg/Kg Maintenance Dose Weekly from Day 8

- Infuse IV over 30 minutes (longer, if hypersensitivity reaction), then observe for 30 minutes
- Mix in 250mL solution (Normal Saline, do **NOT** mix in 5% Dextrose)

REPEAT EVERY 7 DAYS - Until Disease Progression

SUPPORTIVE CARE ANTIEMETIC REGIMEN: NONE HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

GUIDELINE

See the CCNS Website
www.cancercare.ns.ca for the guideline
on Trastuzumab for advanced breast
cancer

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

PATIENT VISIT
CHEMOTHERAPY PATIENT VISIT:
First Visit- Approximately 3 hours
Other Visits- Approximately 1 hour

CLINICAL MONITORING

- Close observation for infusion-related symptoms, including fever, chills, pain (including pain in tumour), asthenia, and other flu-like symptoms. If treatment is well-tolerated during loading dose and early maintenance doses, observation times may be reduced.
- Baseline and periodic **cardiac tests** for all patients with cardiac risk factors or patients with suspected cardiac toxicity

CARDIAC

0. None
1. —
2. Asymptomatic, resting ejection fraction decline by >10% baseline; or abnormal cardiac function tests (LVEF >50) with no baseline for comparison
3. Mild Congestive Heart Failure, responds to therapy
4. Severe/refractory Congestive Heart Failure

BR-TRAST

DOSING CALCULATION TABLE

Loading Dose & Maintenance Dose in mg/mL (Trastuzumab)

Weight (Kg)	40-45	46-50	51-55	56-60
Loading Dose	170/8.1	189/9.0	210/10.0	231/11.0
Maintenance	84/4.0	94.5/4.5	105/5.0	115.5/5.5
Weight (Kg)	61-65	66-70	71-75	76-80
Loading Dose	250/11.9	271/12.9	290/13.8	311/14.8
Maintenance	126/6.0	134.4/6.4	145/6.9	155.4/7.4
Weight (Kg)	81-85	86-90	91-95	96-100
Loading Dose	330/15.7	351/16.7	370/17.6	391/18.6
Maintenance	166/7.9	174.3/8.3	185/8.8	195.3/9.3
Weight (Kg)	101-105	106-110	111-115	116-120
Loading Dose	409.5/19.5	430.5/20.5	449.4/21.4	470.4/22.4
Maintenance	206/9.8	214.2/10.2	225/10.7	235.2/11.2

BR

BR-VINOR

Vinorelbine Chemotherapy

(Advanced Breast Cancer)

**INTERMEDIATE LEVEL
REGIMEN**- Regional Hospital with
Dedicated Cancer Treatment Unit

BR

VINORELBINE 30mg/m² IV Day 1 & Day 8 (or Day 15) (Round to nearest 1mg)

May reduce dose to 25mg/m² IV (for frail, elderly or heavily-pretreated patients)

- Slow push through sidearm of free flowing IV (Normal Saline 250mL); Infuse over 6-10 minutes; infuse balance of IV bag
- If extravasation occurs during administration, discontinue immediately and infuse the remaining dose through another IV site (into another vein)

REPEAT EVERY 21 DAYS - May give Days 1, 8 & 15 every 28 days,
or weekly until blood counts below threshold

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- May give Dopamine Receptor Antagonist PO before chemotherapy (Prochlorperazine 10mg PO or Metoclopramide 10-20mg PO)
- After chemotherapy, use Prochlorperazine 10 mg PO q4-6h PRN, or Metoclopramide 10 mg PO q4h PRN

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, notify physician and **HOLD** dose (Until ANC ≥ 1.5 x 10⁹/L)

Hepatic dysfunction

1. If AST = 60-180IU/L or Bili = 36-50µmol/L, **reduce** Vinorelbine to **50%** dose
2. If AST > 180IU/L or Bili > 50µmol/L, **reduce** Vinorelbine to **25%** dose

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum uric acid levels before each cycle of treatment
- Baseline liver function tests [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]
- Neurologic toxicity ratings (Sensory, Constipation) at each visit
- Watch for symptoms of fever or infection

CONSTIPATION

0. No change
2. Mild
3. Moderate
4. Severe
4. Ileus >96 hours

SENSORY

0. No change
 1. Mild paraesthesia; no deep tendon reflex
 2. Mild/moderate sensory loss; moderate paraesthesia
 3. Sensory loss interferes with function
- Rated at each clinic visit**

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:

Approx. 30 minutes

BR-VINOR-TRAST

Vinorelbine-Trastuzumab Chemotherapy

(Treatment of Advanced Breast Cancer in Women whose Tumours Overexpress the HER2 Protein)

**First Cycle -
INTERMEDIATE LEVEL REGIMEN-**
Regional Hospital with Dedicated
Cancer Treatment Unit

**Other Cycles (if no reaction) -
BASIC LEVEL REGIMEN-**
Community Hospital with
Oncology Nurses

VINORELBINE 30mg/m² IV Day 1 & Day 8 (or Day 15) (Round to nearest 1mg)

May reduce dose to 25mg/m² IV (for frail, elderly or heavily-pretreated patients)

- Slow push through sidearm of free flowing IV (Normal Saline 250mL); Infuse over 6-10 minutes; infuse balance of IV bag
- If extravasation occurs during administration, discontinue immediately and infuse the remaining dose through another IV site (into another vein)

REPEAT EVERY 21 DAYS - May give Days 1, 8 & 15 every 28 days, or weekly until blood counts below threshold

PREMEDICATIONS:

May give ACETAMINOPHEN 650mg PO and/or DIPHENHYDRAMINE 50mg PO

TRASTUZUMAB 4mg/Kg Loading Dose Day 1 Only

DO NOT ADMINISTER AS IV PUSH OR BOLUS

- Mix in 250mL solution (Normal Saline, do NOT mix in 5% Dextrose)
- Infuse IV over 90 minutes, then observe for 60 minutes

2mg/Kg Maintenance Dose Weekly from Day 8

- Infuse IV over 30 minutes (longer, if hypersensitivity reaction), then observe for 30 minutes
- Mix in 250mL solution (Normal Saline, do NOT mix in 5% Dextrose)

REPEAT EVERY 7 DAYS - Until Disease Progression

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

Vinorelbine Days- LOW RISK

- May give Dopamine Receptor Antagonist PO before chemotherapy (Prochlorperazine 10mg PO or Metoclopramide 10-20mg PO)
- After chemotherapy, use Prochlorperazine 10 mg PO q4-6h PRN, or Metoclopramide 10 mg PO q4h PRN

Trastuzumab ONLY Days-

ANTIEMETIC REGIMEN: NONE

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

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BR-VINOR-TRAST

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CLINICAL MONITORING

Trastuzumab Criteria

- Close observation for infusion-related symptoms, including fever, chills, pain (including pain in tumour), asthenia, and other flu-like symptoms. If treatment is well-tolerated during loading dose and early maintenance doses, observation times may be reduced.
- Baseline and periodic cardiac tests for all patients with cardiac risk factors or suspected cardiac toxicity

CARDIAC

0. None

1. —

- 2. Asymptomatic, resting ejection fraction decline by >10% baseline; or abnormal cardiac function tests (LVEF >50) with no baseline for comparison
- 3. Mild Congestive Heart Failure, responds to therapy
- 4. Severe/refractory Congestive Heart Failure

Vinorelbine Criteria

- **Complete blood count including differential, platelets and hemoglobin (CBC) and serum uric acid levels** before each cycle of treatment
- Baseline **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]
- **Neurologic** toxicity ratings (Sensory, Constipation) at each visit
- Watch for symptoms of **fever or infection**

CONSTIPATION

0. No change

2. Mild

3. Moderate

4. Severe

4. Ileus >96 hours

SENSORY

0. No change

1. Mild paraesthesia; no deep tendon reflex

2. Mild/moderate sensory loss; moderate paraesthesia

3. Sensory loss interferes with function

Rated at each clinic visit

GUIDELINE

See the CCNS Website
www.cancercare.ns.ca for the guideline
on Trastuzumab for advanced breast
cancer

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

DOSE MODIFICATION

Vinorelbine Treatments:

- If ANC < 1.5 x 10⁹/L, notify physician
and **HOLD** dose

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:

First Trastuzumab Treatment Visit-

Approximately 3 hours

Other Trastuzumab **ONLY** Treatment

Visits- Approximately 1 hour

Approx. 6 hours

Trastuzumab/Vinorelbine Treatment

Visits- Approximately 1 1/2 hours

BR-VINOR-TRAST

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DOSING CALCULATION TABLE

Loading Dose & Maintenance Dose in mg/mL (Trastuzumab)

Weight (Kg)	40-45	46-50	51-55	56-60
Loading Dose	170/8.1	189/9.0	210/10.0	231/11.0
Maintenance	84/4.0	94.5/4.5	105/5.0	115.5/5.5
Weight (Kg)	61-65	66-70	71-75	76-80
Loading Dose	250/11.9	271/12.9	290/13.8	311/14.8
Maintenance	126/6.0	134.4/6.4	145/6.9	155.4/7.4
Weight (Kg)	81-85	86-90	91-95	96-100
Loading Dose	330/15.7	351/16.7	370/17.6	391/18.6
Maintenance	166/7.9	174.3/8.3	185/8.8	195.3/9.3
Weight (Kg)	101-105	106-110	111-115	116-120
Loading Dose	409.5/19.5	430.5/20.5	449.4/21.4	470.4/22.4
Maintenance	206/9.8	214.2/10.2	225/10.7	235.2/11.2

REGIMEN CONTENTS**EN-MITOT** - *Mitotane* Chemotherapy**EN-OCTREO** - Octreotide Therapy 290**EN-STREP-DOXO** - Streptozocin-
Doxorubicin Chemotherapy 291**EN-STREP-FU** - Streptozocin-
Fluorouracil Chemotherapy 293

EN

NOTE: *Regimen names in italics* are not in this pocketbook version- See full version for regimen monograph

EN-OCTREO

Octreotide Therapy

(Carcinoid Syndrome, VIPomas,
Glucagonomas, GRFomas- Palliative
Intent)

**Take-Home Prescription-
Special Authorization Required**

OCTREOTIDE 50-150mcg BID - TID SC

(Outpatient prescription in multiples of 50mcg, 150mcg & 500mcg vials)

CONTINUOUS TREATMENT

SUPPORTIVE CARE
ANTIEMETIC REGIMEN: NONE

NOTE

- Prescription covered by some third party prescription plans
- Dispense medication with adequate number of syringes, needles, alcohol swabs and other equipment for patient self-injection

CLINICAL MONITORING

- Baseline and periodic **serum glucose levels**, especially in diabetic patients
- **Ultrasonograph of the gall bladder**, to assess the presence of gallstones (during long-term therapy)

EN-STREP-DOXO

Streptozocin-Doxorubicin Chemotherapy

(Islet Cell Carcinoma- Palliative Intent)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

STREPTOZOCIN 1000mg/m² IV Days 1 to 5 in first cycle

1500-2000mg/m² IV Day 1 subsequent cycles (Round to nearest 10mg)

- Mix in 50mL bag (Normal Saline); Infuse over 15-30 minutes through rapid free-flowing IV

DOXORUBICIN 50mg/m² IV Days 1 & 22 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV over at least 3-5 minutes
- Slow down injection rate if erythematous streaking occurs

REPEAT EVERY 42 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

INTERMEDIATE RISK

Pre-Chemotherapy:

- Serotonin Receptor Antagonist IV (Ondansetron 8mg IV pre-chemo & 8mg PO qhs on Days 1 to 5 & Day 22, OR Granisetron 1mg IV pre-chemo Days 1 to 5 & Day 22, OR Dolasetron 100mg IV pre-chemo Days 1 to 5 & Day 22). **AND**
- Dexamethasone 8mg IV pre-chemo Days 1 to 5 (may increase to 20mg PO or IV)

Post-Chemotherapy:

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
- No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
- Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo **AND**
- Dexamethasone 8mg PO q24h for 2 doses
- Prochlorperazine 10mg PO (or 10mg PR) q4h PRN

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Renal failure (Suggested action)

1. If Creatinine Clearance = 12-48ml/min, **reduce** Streptozocin to **75%** dose
2. If Creatinine Clearance < 12ml/min, **reduce** Streptozocin to **50%** dose
3. If Serum Creatinine > 265µmol/L, **reduce** Doxorubicin to **50%** dose

Hepatic dysfunction (Suggested action)

1. If Bili=26-51µmol/L or AST=60-180IU/L, **reduce** Doxorubicin to **50%** dose
1. If Bili > 85µmol/L or AST > 180IU/L, **reduce** Doxorubicin to **25%** dose
1. If Bili > 85µmol/L or AST > 180IU/L, **Omit** dose of both drugs

NOTE

- Notify Pharmacy in advance. Streptozocin is not usually kept in stock, and will require a few days to obtain.

EN-STREP-DOXO

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Baseline & periodic **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated], **serum glucose levels** & **serum cortisol levels**
- Clinical exam for symptoms of **Congestive Heart Failure**
- Baseline and periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels [Echocardiograms, WMS studies, and/or all angiography scans]
- Baseline **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]
- Periodic **neurological assessments** (after 2 years' treatment)
- Local Site Toxicity ratings, if incident of phlebitis

LOCAL SITE TOXICITY

- 0 None
- 1 Pain
- 2 Pain & inflammation; phlebitis
- 3 Ulceration
- 4 Plastic surgery

Upon Patient Complaint Or Clinical Event

CARDIAC

- 0 None
- 1 —
- 2 Asymptomatic, resting ejection fraction decline by >10% baseline, or abnormal cardiac function tests (LVEF >50) with no baseline for comparison
- 3 Mild Congestive Heart Failure, responds to therapy
- 4 Severe/refractory Congestive Heart Failure

At cumulative dose threshold and subsequent intervals

For Cardiac Toxicity Ratings:

First rating at baseline, then at the cumulative dose **threshold** of 300mg/m², & repeat ratings at each cumulative dose **increment** of 100mg/m² above threshold (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation)

Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given: cardiotoxicity is additive

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT

Approx. 45-60 minutes

EN-STREP-FU

Streptozocin-Fluorouracil Chemotherapy

(Metastatic Carcinoid, Insulinoma-
Palliative Intent, Second Line Therapy)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

STREPTOZOCIN 500mg/m² IV daily for 5 days (Round to nearest 10mg)

- Mix in 50mL bag (Normal Saline); Infuse over 15 minutes through rapid free-flowing IV

FLUOROURACIL 400-500mg/m² IV daily for 5 days

(Round to nearest 25mg)

- Inject by slow push through sidearm of free flowing IV
- May give by direct IV push, followed by a Normal Saline flush, if no IV line has been set up

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: INTERMEDIATE RISK

Pre-Chemotherapy:

- Serotonin Receptor Antagonist IV (Ondansetron 8mg IV pre-chemo & 8mg PO qhs on Days 1 to 5, OR Granisetron 1mg IV pre-chemo Days 1 to 5, OR Dolasetron 100mg IV pre-chemo Days 1 to 5), **AND**
- Dexamethasone 8mg IV pre-chemo Days 1 to 5 (may increase to 20mg PO or IV)

Post-Chemotherapy:

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
- No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
- Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo **AND**
- Dexamethasone 8mg PO q24h for 2 doses
- Prochlorperazine 10mg PO (or 10mg PR) q4h PRN

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Renal failure (Suggested action)

1. If CrCl = 12-48mL/min, reduce Streptozocin to **75%** dose
2. If CrCl < 12mL/min, reduce Streptozocin to **50%** dose

Hepatic dysfunction (Suggested action)

1. If Bili > 85µmol/L or AST > 180IU/L, **Omit** dose

CLINICAL MONITORING

- Baseline and regular **renal function tests** (serum creatinine, electrolytes & BUN)
- **Urinalysis** (for proteinuria)
- Clinical assessment of **stomatitis**, oral examination upon patient complaint of a sore mouth

NOTE

- Notify Pharmacy in advance. Streptozotocin is not usually kept in stock, and will require a few days to obtain.

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:
Approx. 45-60 minutes

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NOTE

The combination of 5FU with LEVAMISOLE is no longer recommended for treatment of colorectal cancer. 5FU-Leucovorin regimens are recommended for equivalent outcomes with reduced toxicity.

NOTE: Regimen names in italics are not in this pocketbook version- See full version for regimen monograph

GI-CAPECIT

Capecitabine Therapy

(Advanced Colorectal Cancer)

(Xeloda™ is the Brand Name for
Capecitabine)

**Take-Home Prescription-
Special Authorization Required**

CAPECITABINE 1000-1250mg/m² PO BID for 14 days

(Outpatient prescription in multiples of 150mg & 500mg tablets)

- Take capsules WITH FOOD; may divide dose into 3 or 4 divided doses if poorly tolerated
- Prophylaxis To Prevent Hand-Foot Skin Reaction:
 1. Take Pyridoxine (Vitamin B6) 100mg BID or 50mg TID continuously
 2. Apply a hydrating lotion or cream (e.g. Bag Balm, Udder Cream) to hands & feet once or twice daily

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- May give Prochlorperazine 10mg
PO(and/or PR) q4-6h PRN

OTHER SUPPORTIVE CARE:

Diarrhea

Loperamide 4mg PO at the onset of diarrhea, then 2mg q2h PO until patient is diarrhea-free for 12 hours (May take 4mg q4h at night for convenience)

CLINICAL MONITORING

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Clinical assessment of stomatitis:** oral examination upon patient complaint of a sore mouth
- **Skin assessment**, especially extremities
- Routine assessment of **Diarrhea**, at each clinic visit and telephone reinforcement

DIARRHEA

- 0 None
- 1. Increase of 2-3 stools/day over pretreatment
- 2. Increase of 4-6 stools/day or nocturnal stools
- 3. Increase of 7-9 stools/day, incontinence, malabsorption
- 4. Increase of ≥ 10 stools/day, grossly bloody diarrhea, need for parenteral nutrition support

HAND-FOOT SKIN REACTION

- 0 None
- 1. Skin changes or dermatitis without pain
- 2. Skin changes with pain, **not** interfering with function
- 3. Skin changes with pain, interfering with function
- 4. ———

Rated at each clinic visit

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GI-CAPECIT

DOSE MODIFICATION

Gastrointestinal or Skin Toxicities

1 If any Toxicity Score = Grade 2

HOLD Capecitabine until score = 0 or 1, resume at 100% dose (if second occurrence, resume at 75% dose, third occurrence at 50%, if fourth occurrence **STOP** Capecitabine)

2 If any Toxicity Score = Grade 3

HOLD Capecitabine until score = 0 or 1, resume at 75% dose or 1000mg/m² BID (if second occurrence, resume at 50%, if third occurrence **STOP** Capecitabine)

3 If any Toxicity Score = Grade 4

STOP Capecitabine
If needed, Pharmacy can assist in calculation for dosage reductions

NOTE

- Prescription costs covered by most third party prescription plans
- *Pharmacare patients will require a physician letter, requesting approval for coverage*
- The cost per treatment course (i.e. 14 days) can range from \$700-1,100, depending upon patient

GUIDELINE

See the CCNS Website
www.cancercare.ns.ca for the guideline on Capecitabine for Breast cancer

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

DOSING CALCULATION TABLE (1250mg/m² dose)

BSA	≤1.24	1.25	1.37	1.52	1.65	1.77	1.92	2.05	≥2.18
		-1.36	-1.51	-1.64	-1.76	-1.91	-2.04	-2.17	
Daily Dose	3000 mg	3300 mg	3600 mg	4000 mg	4300 mg	4600 mg	5000 mg	5300 mg	5600 mg
				<u>Tablets per dose</u>					
150mg	0	1	2	0	1	2	0	1	2
500mg	3	3	3	4	4	4	5	5	5

DOSING CALCULATION TABLE (1000mg/m² dose)

BSA	≤1.22	1.23	1.40	1.58	1.73	1.90	2.08	2.23	≥2.40
		-1.39	-1.57	-1.72	-1.89	-2.07	-2.22	-2.39	
Daily Dose	2300 mg	2600 mg	3000 mg	3300 mg	3600 mg	4000 mg	4300 mg	4600 mg	5000 mg
				<u>Tablets per dose</u>					
150mg	1	2	0	1	2	0	1	2	0
500mg	2	2	3	3	3	4	4	4	5

GI-ECF

Epirubicin-Cisplatin- Fluorouracil Chemotherapy

(Advanced Gastric Carcinoma-
Palliative Intent)

**INTERMEDIATE LEVEL
REGIMEN-** Regional Hospital with
Dedicated Cancer Treatment Unit

PREHYDRATION Day 1

- Encourage patients to drink 6-8 glasses of water prior to chemo each day (increase fluids if poorly hydrated)
- May give 1000mL Normal Saline; infuse over 1 hour

EPIRUBICIN 50mg/m² IV Day 1 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV

CISPLATIN 60mg/m² IV Day 1 (Round to nearest 1mg- Max. dose=150mg)

- Mix drug in 500mL Normal Saline; Infuse over 60 minutes (increase fluids if poor oral intake)
- May add Mannitol 20g (200mL of 10% Solution); infuse through sidearm concurrently

5-FLUOROURACIL 200mg/m²/Day CIV for 21 weeks Starting on Day 1

- Continuous infusion using ambulatory infusion pump (Round to nearest 50mg- Max. 2g/day)
- Infuse through patent central venous catheter; Inspect infusion site weekly and replace if evidence of extravasation or infection

POSTHYDRATION Day 1

- May give 1000mL Normal Saline; infuse over 1 hour
- Increase fluids if poor oral intake

REPEAT DAY 1 TREATMENTS EVERY 21 DAYS- CONTINUOUS INFUSION FOR 21 WEEKS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *When available in Canada*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)

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GI-ECF

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Baseline and routine **renal function tests** [serum creatinine, electrolytes & BUN]
- Clinical exam for symptoms of **Congestive Heart Failure**
- Periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels
- Baseline **liver function tests** (especially if poor Performance Status) (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated)
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Skin assessment**, especially extremities
- Hearing & Neurologic toxicity ratings (Sensory)-each visit

HEARING

0. No change
1. Asymptomatic
2. Tinnitus
3. Correctable hearing loss
4. Deafness

SENSORY

0. No change
1. Mild paraesthesia, no deep tendon reflex
2. Mild/moderate sensory loss, moderate paraesthesia
3. Sensory loss interferes with function

Rated at each clinic visit

DOSE MODIFICATION

Hematologic Toxicities:

1. If ANC < $1.5 \times 10^9/L$, or if Platelets < $100 \times 10^9/L$, notify physician and **REDUCE** to **50%** dose (may reduce 5FU CIV dose also)
2. If ANC < $1.0 \times 10^9/L$ **OR** if Platelets < $75 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Gastrointestinal Toxicities:

1. If Mucositis or Diarrhea $\geq$ Grade 3 in previous course, **REDUCE** to **50%** dose of 5-FU

Renal failure (Recommended action)

1. If Renal Function has not returned to normal (CrCl > 60mL/min or Serum Creatinine > 136 μ mol/L) by Day 1 of cycle, **DISCONTINUE CISPLATIN**
2. If Serum Creatinine > 265 μ mol/L, **Reduce** Epirubicin to **50%** dose

Hepatic dysfunction (Suggested action)

1. If Bili=26-51 μ mol/L or AST =60-180IU/L, give **50%** of Epirubicin dose
2. If Bili= 52-85 μ mol/L or AST>180IU/L, give **25%** of Epirubicin dose
3. If Bili >85 μ mol/L, **OMIT** all drugs

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:

Day 1-Approx 1/2 to 3 hours
(depending upon hydration)

Days 8,15 &22- Approx. 45 min

GI-EPI-CARBO-FU

Epirubicin-Carboplatin- Fluorouracil Chemotherapy

(Advanced Gastric Carcinoma-
Palliative Intent)

**INTERMEDIATE LEVEL
REGIMEN-** Regional Hospital with
Dedicated Cancer Treatment Unit

PREHYDRATION Day 1

- Encourage patients to drink 6-8 glasses of water prior to chemo each day (increase fluids if poorly hydrated)

EPIRUBICIN 50mg/m² IV Day 1 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV

CARBOPLATIN AUC= 6mg/mL/min IV Day 1 (Round to nearest 1mg)

- Mix in 250mL bag (5% Dextrose); Infuse over 30 minutes

5-FLUOROURACIL 200mg/m²/day CIV for 21 weeks Starting on Day 1

- Continuous infusion using ambulatory infusion pump
- Infuse through patent peripheral venous catheter; Inspect peripheral infusion sites daily and replace if evidence of irritation or extravasation (Round to nearest 50mg- Max. 2g/day)

REPEAT DAY 1 TREATMENTS EVERY 21 DAYS- CONTINUOUS INFUSION FOR 21 WEEKS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV). **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses. **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
- No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
- Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *When available in Canada*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)

NOTE

Calvert AUC Dosing Formula

DOSE (mg)=target AUC x (GFR + 25)

- GFR expressed as measured Creatinine clearance (mL/min) or estimated from serum Creatinine

Creatinine Clearance (X60 for mL/min)

$$Cl_{cr} \text{ ♂ (mL/sec) } = \frac{140 - \text{age(yrs)} \times \text{TBW (kg)}}{50 \times Cr_{\text{Serum}} (\mu\text{mol/L})}$$

$$Cl_{cr} \text{ ♀ (mL/sec) } = Cl_{cr} \text{ ♂} \times 0.85$$

Continued Next Page

GI-EPI-CARBO-FU

CLINICAL MONITORING

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- Baseline and periodic **renal function tests** [serum creatinine, electrolytes & BUN]
- Clinical exam for symptoms of **Congestive Heart Failure**
- Periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels (especially if poor Performance Status)
- Baseline **liver function tests** (especially if poor Performance Status) (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels)
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Skin assessment**, especially extremities
- **Neurologic toxicity ratings** (Sensory)- each visit

SENSORY

0.No change

1.Mild paraesthesia; no deep tendon reflex

2 Mild/moderate sensory loss; moderate paraesthesia

3.Sensory loss interferes with function

Rated At Each Clinic Visit

DOSE MODIFICATION

Hematologic Toxicities:

1. If ANC < $1.5 \times 10^9/L$, or if Platelets < $100 \times 10^9/L$, notify physician and **REDUCE to 50%** dose (may reduce 5FU CIV dose also)
2. If ANC < $1.0 \times 10^9/L$ OR if Platelets < $75 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Gastrointestinal Toxicities:

1. If Mucositis or Diarrhea $\geq$ Grade 3 in previous course, **REDUCE to 50%** dose of 5-FU

Renal failure (*Recommended action*)

1. If Serum Creatinine= $136-150\mu\text{mol/L}$ or Creatinine Clearance = $40-60\text{mL/min}$; **reduce** Carboplatin dose by **1mg/mL/min** (or by **50mg/m^2** for BSA dosing)
2. If Serum Creatinine= $151-180\mu\text{mol/L}$ or Creatinine Clearance = $20-40\text{mL/min}$; **reduce** Carboplatin dose by **2mg/mL/min** (or by **100mg/m^2** for BSA dosing)
3. If Serum Creatinine $>181\mu\text{mol/L}$ or CrCl < 20mL/min , **DISCONTINUE** Carboplatin dose
4. If if Bili $>85\mu\text{mol/L}$, **Omit** Epirubicin dose

Hepatic dysfunction (*Suggested action*)

1. If Bili= $26-51\mu\text{mol/L}$ or AST = $60-180\text{IU/L}$, give **50%** of Epirubicin dose
2. If Bili= $52-85\mu\text{mol/L}$ or AST $>180\text{IU/L}$, give **25%** of Epirubicin dose
3. If Bili $>85\mu\text{mol/L}$, **OMIT** all drugs

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

PATIENT VISIT
CHEMOTHERAPY PATIENT VISIT:
Approx. 1 1/2 to 2 hours

[Rev 05/02]

GI-ELF

Etoposide-Leucovorin- Fluorouracil (ELF) Chemotherapy

(Metastatic Gastric Carcinoma-
Palliative Intent)

INTERMEDIATE LEVEL REGIMEN-

Community Hospital with
Oncology Nurses

LEUCOVORIN 200mg/m² IV Days 1 to 3 (Round to nearest 1mg)

- Mix in 100mL bag (5% Dextrose or Normal Saline); infuse through sidearm of free-flowing IV over 15 minutes

ETOPOSIDE 120mg/m² IV Days 1 to 3 (Round to nearest 10mg)

- Mix in 500mL bag (5% Dextrose or Normal Saline); (if Etoposide dose >200mg, mix in 600mL bags); connect piggyback to IV line; After Leucovorin completed, infuse over 60 minutes; Adjust rate if blood pressure drops

5-FLUOROURACIL 500mg/m² IV Days 1 to 3 (Round to nearest 25mg)

- Give by push through sidearm of free flowing IV (Normal Saline or 5% Dextrose)

REPEAT EVERY 21-28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: INTERMEDIATE RISK

Pre-Chemotherapy- Days 1 to 3

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO pre-chemo & 8mg PO qhs on Days 1 to 3, OR Granisetron 2mg PO pre-chemo Days 1 to 3, OR Dolasetron 100mg IV pre-chemo Days 1 to 3), **AND**
- Dexamethasone 8mg IV pre-chemo Days 1 to 3 (may increase to 20mg PO or IV)

Post-Chemotherapy-

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses, OR Granisetron 1mg PO q24h for 1-2 doses, OR Dolasetron 100mg PO q24h for 1-2 doses, **AND**
- Dexamethasone 8mg PO q24h for 2 doses
- Prochlorperazine 10mg PO (or 10mg PR) q4h PRN
- Patients **recommended** to suck on ice chips during bolus injection, to reduce stomatitis

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

Continued Next Page...

GI-ELF**CLINICAL MONITORING**

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth
- Baseline liver function tests (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated) & renal function tests [serum creatinine, electrolytes & BUN]
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth
- Baseline blood pressure at each treatment; monitor for hypotension

DOSE MODIFICATIONHematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$ OR if Platelets $< 100 \times 10^9/L$, notify physician and **REDUCE** to **50%** dose
2. If ANC $< 1.0 \times 10^9/L$ OR if Platelets $< 75 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Gastrointestinal Toxicities

1. If Mucositis or Diarrhea $\geq$ Grade 3 in previous course, **REDUCE** to **50%** dose

Hepatic dysfunction (*Suggested action*)

1. If Bili=26-51 μ mol/L or AST=60-180IU/L, reduce Etoposide to **50%** dose
2. If Bili= 52-85 μ mol/L, reduce Etoposide to **25%** dose
3. If bilirubin elevated above 85 μ mol/L (marked hepatic dysfunction) , **OMIT** dose

Renal dysfunction (*Suggested action*)

1. If CrCl =12-48mL/min or Serum Creatinine > 130 mmol/L, reduce Etoposide to **75%** dose
2. If CrCl < 12 mL/min, reduce Etoposide to **50%** dose

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

PATIENT VISIT
CHEMOTHERAPY PATIENT VISIT:
Approximately 90 minutes

5-Fluorouracil Chemotherapy

(Rectal Carcinoma)

BASIC LEVEL REGIMEN-
Community Hospital with
Oncology Nurses

5-FLUOROURACIL 500mg/m² IV Days 1 to 5 (Round to nearest 25mg)
1 to 3 During First & Last (Fifth) Week of Radiotherapy;

Then 450mg/m² IV Days 1 to 5 After Radiotherapy

- Inject by direct IV push, followed by a Normal Saline flush, if no IV line has been set up
- May give by slow push through sidearm of free flowing IV

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic before chemotherapy
- After chemotherapy, use Prochlorperazine 10 mg PO q4-6h PRN, or Metoclopramide 10 mg PO q3-4h

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < $1.5 \times 10^9/L$, or if Platelets = $75-100 \times 10^9/L$, notify physician and **REDUCE 5FU to 50% dose**
2. If ANC < $1.0 \times 10^9/L$ OR if Platelets < $75 \times 10^9/L$, notify physician and **HOLD dose for 1 week**

Gastrointestinal Toxicities

1. If Mucositis or Diarrhea $\geq$ Grade 3 in previous course, **REDUCE to 50% dose**

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth
- Baseline liver function tests (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated) & renal function tests [serum creatinine, electrolytes & BUN] (if severe organ failure suspected)

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:
Approx. 30 minutes

[Rev. 05/01]

GI-FU*ADJ

5-Fluorouracil (IV-CIV-IV)

Chemotherapy

(Rectal Carcinoma Curative Intent
[Neoadjuvant/Adjuvant to
Radiotherapy])

BASIC LEVEL REGIMEN-

Community Hospital with
Oncology Nurses

ADVANCED LEVEL REGIMEN-

(During Radiotherapy ONLY)
Provincial Cancer Centre

5-FLUOROURACIL 500mg/m² IV Days 1 to 5

- Inject by direct IV push, followed by a Normal Saline flush, if no IV line has been set up (Round to nearest 25mg)
- May give by slow push through sidearm of free flowing IV

REPEAT EVERY 28 DAYS (2 cycles before Radiotherapy)

Followed by:

5-FLUOROURACIL 225mg/m²/Day CIV for 35 days

Starting on day 1 of radiotherapy (5000cGy/25 fractions over 5 weeks)

- Continuous infusion using ambulatory infusion pump (Round to nearest 50mg- Max. 2g/day)
- Infuse through central venous access device, if available
- Protect from light

Followed by:

5-FLUOROURACIL 450mg/m² IV Days 1 to 5

(Round to nearest 25mg)

- Inject by direct IV push, followed by a Normal Saline flush, if no IV line has been set up
- May give by slow push through sidearm of free flowing IV

REPEAT EVERY 28 DAYS (2 cycles after Radiotherapy)

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic before chemotherapy
- After chemotherapy, use Prochlorperazine 10 mg PO q4h PRN, or Metoclopramide 10 mg PO q3-4h PRN
- Patients *recommended* to suck on ice chips during bolus injection and for 30 minutes after, to reduce

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets = 75-100 x 10⁹/L, notify physician and **REDUCE** 5FU to **50%** dose
2. If ANC < 1.0 x 10⁹/L OR if Platelets < 75 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Gastrointestinal Toxicities

1. If Mucositis or Diarrhea ≥ Grade 3 in previous course, **REDUCE** to **50%** dose

Hepatic dysfunction

1. If bilirubin elevated above 85µmol/L (marked hepatic dysfunction), **OMIT** dose
(Suggested action)

GI-FU*ADJ

CLINICAL MONITORING

- **Complete blood count** including differential, platelets and hemoglobin (CBC) before each cycle of treatment & weekly during continuous infusion
- **Clinical assessment of stomatitis**, oral examination upon patient complaint of a sore mouth
- **Baseline liver function tests** (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated) & **renal function tests** [serum creatinine, electrolytes & BUN] (if severe organ failure suspected)
- **Clinical assessment of stomatitis**, oral examination upon patient complaint of a sore mouth
- **Skin assessment**, especially extremities phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated) & **renal function tests** [serum creatinine, electrolytes & BUN] (if severe organ failure suspected)
- **Clinical assessment of stomatitis**, oral examination upon patient complaint of a sore mouth
- **Skin assessment**, especially extremities

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT

5FU IV Bolus Days = Approx. 15 minutes

5FU IV Pump Days = Approx. 30 minutes

GI-FU-CISP

5-Fluorouracil Infusion/ Cisplatin Chemotherapy

(Combined Modality: Carcinoma of the
Esophagus)

PREHYDRATION

- Encourage patient to drink 6-8 glasses of water prior to chemo each day (increase fluids if poorly hydrated)
- May give 1000mL Normal Saline; infuse over 1 hour

CISPLATIN 75mg/m² IV Day 1 (Round to nearest 1 mg)

- Mix drug in 500ml bag (Normal Saline); Infuse over 1 hour
- May admix 20G Mannitol (200mL of 10% solution) with Cisplatin

POSTHYDRATION

- May give 1000mL Normal Saline; Infuse over 1 hour

5-FLUOROURACIL 1000mg/m² day CIV for 96 hours

- Starting on Day 1 (Round to nearest 50mg- Max. 2g/day)
 - Admin in 1000mL Normal Saline and administer by Continuous Infusion over 96 hours (Inpatient treatment), or
 - Continuous infusion using ambulatory infusion pump (Outpatient treatment)
 - Infuse through patent peripheral venous catheter; Inspect peripheral infusion sites daily and replace if evidence of irritation or extravasation
- During WEEKS 1 & 5 of Radiotherapy, then **REPEAT EVERY 28 DAYS**

INTERMEDIATE LEVEL REGIMEN

Regional Hospital with Dedicated
Cancer Treatment Unit

Alternate CISPLATIN Dosing

PREHYDRATION

- Encourage patients to drink 6-8 glasses of water prior to chemo each day
- May prehydrate with 1000mL Normal Saline; Infuse over 60 minutes

CISPLATIN 25mg/m² IV Days 1,2&3 (Round to nearest 1 mg)

- Mix drug in 250mL bag (Normal Saline); Infuse over 30 minutes

POSTHYDRATION

- May give 500mL Normal Saline; Infuse over 30 minutes

SUPPORTIVE CARE

ANTIEMETIC REGIMEN HIGH RISK

- Serotonin Receptor Antagonist IV (Ondansetron 8mg IV q12h on Day 1, OR Granisetron 1mg IV, OR Dolasetron 100mg IV) AND
- Dexamethasone 20mg IV

Post-Chemotherapy:

- Dexamethasone 8 mg PO q24h for 3 days AND
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses, OR Granisetron 2mg PO q24h for 2 doses, or Dolasetron 100mg PO q24h for 2 doses)
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO/PR PRN or Metoclopramide 10mg PO PRN)

Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration

GI-FU-CISP

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Baseline and routine renal function tests [serum creatinine, serum electrolytes (including magnesium, calcium, potassium levels)] before each treatment cycle
- Clinical assessment of stomatitis: oral examination upon patient complaint of a sore mouth
- Skin assessment, especially extremities
- Baseline liver function tests [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]
- Hearing & Neurologic toxicity ratings (Sensory)- each visit

HEARING

0 No change

1 Asymptomatic

2 Tinnitus

3 Correctable hearing loss

4 Deafness

SENSORY

0 No change

1 Mild paraesthesia, no deep tendon reflex

2 Mild/moderate sensory loss, moderate paraesthesia

3 Sensory loss interferes with function

Rated at each clinic visit

DOSE MODIFICATION

Hematologic Toxicities:

1. If ANC < $1.5 \times 10^9/L$, or if Platelets = $75-100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Gastrointestinal Toxicities:

1. If Mucositis or Diarrhea $\geq$ Grade 3 in previous course, **REDUCE** to **50%** dose of 5-FU

Renal failure

1. If Renal Function has not returned to normal (CrCl > 60mL/min or Serum Creatinine < 136 μ mol/L) by Day 1 of cycle, **DISCONTINUE**

CISPLATIN

(Recommended action)

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:

Days 1 to 3 = 3 to 4 hours (depending upon hydration)

Day 5 = 15 minutes

GI-FU-LEUC

5-Fluorouracil-Leucovorin Chemotherapy

(Advanced Colorectal/Gastric
Carcinoma: Adjuvant Rectal
Carcinoma)

BASIC LEVEL REGIMEN-
Community Hospital with
Oncology Nurses

LEUCOVORIN 20mg/m² IV Days 1 to 5 (Round to nearest 1mg)

- Inject by direct IV push, followed by a Normal Saline flush, if no IV line has been set up
- May give by slow push through sidearm of free flowing IV (Normal Saline)

5-FLUOROURACIL 425mg/m² IV Days 1 to 5 (Round to nearest 25mg)

- Inject by direct IV push, followed by a Normal Saline flush, if no IV line has been set up
- May give by slow push through sidearm of free flowing IV

REPEAT EVERY 28 DAYS (Adjuvant-For a Total of 6 Months)

DURING CONCURRENT RADIOTHERAPY ADMINISTRATION:

Give 5-FLUOROURACIL & LEUCOVORIN on Days 1 to 4 ONLY

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic before chemotherapy
- May give Dopamine Receptor Antagonist PO before chemotherapy (Prochlorperazine 10mg PO or Metoclopramide 10-20mg PO)
- After chemotherapy, use Prochlorperazine 10 mg PO q4h PRN, or Metoclopramide 10 mg PO q4h PRN
- Patients **recommended** to suck on ice chips during bolus injection and for 30 minutes after, to reduce stomatitis

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Gastrointestinal Toxicities

1. If Mucositis or Diarrhea ≥ Grade 3 in previous course, **REDUCE** to **50%** dose

Hepatic dysfunction (Suggested action)

1. If bilirubin elevated above 85μmol/L (marked hepatic dysfunction), **OMIT** dose

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth
- Baseline liver function tests (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated) & renal function tests [serum creatinine, electrolytes & BUN] (if severe organ failure suspected)
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

NOTE

Lower doses of Fluorouracil are associated with reduced response rates

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:
Approx. 15 minutes

[Rev. 05/01]]

GI-FU-LEUC*W

Weekly 5-Fluorouracil- Leucovorin Chemotherapy

(Advanced Colorectal/Gastric
Carcinoma)

BASIC LEVEL REGIMEN-

Community Hospital with
Oncology Nurses

LEUCOVORIN 20mg/m² IV Day 1 (Round to nearest 1mg)

- Inject by direct IV push, followed by a Normal Saline flush, if no IV line has been set up
- May give by slow push through sidearm of free flowing IV (D5W, Normal Saline)

5-FLUOROURACIL 500mg/m² IV Day 1(Round to nearest 25mg)

- Inject by direct IV push, followed by a Normal Saline flush, if no IV line has been set up
- May give by slow push through sidearm of free flowing IV

REPEAT EVERY 7 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic before chemotherapy
- May give Dopamine Receptor Antagonist PO before chemotherapy (Prochlorperazine 10mg PO or Metoclopramide 10-20mg PO)
- After chemotherapy, use Prochlorperazine 10 mg PO q4h PRN, or Metoclopramide 10 mg PO q4h PRN
- Patients **recommended** to suck on ice chips during bolus injection and for 30 minutes after, to reduce stomatitis

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Gastrointestinal Toxicities

1. If Mucositis or Diarrhea ≥ Grade 3 in previous course, **REDUCE** to 50% dose

Hepatic dysfunction (Suggested action)

1. If bilirubin elevated above 85µmol/L (marked hepatic dysfunction), **OMIT** dose

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Clinical assessment of stomatitis, oral examination upon patient complaint of a sore mouth
- Baseline liver function tests (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated) & renal function tests [serum creatinine, electrolytes & BUN] (if severe organ failure suspected)
- Clinical assessment of stomatitis, oral examination upon patient complaint of a sore mouth

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:
Approx. 15 minutes

GI-FL-FU***CIV22**

5-Fluorouracil-Leucovorin/ 5-Fluorouracil 22 Hour Continuous Infusion (also known as De Gramont LV5FU2 Regimen)

(Advanced Colorectal Carcinoma)

BASIC LEVEL REGIMEN-
Community Hospital with
Oncology Nurses

LEUCOVORIN 200mg/m² IV Days 1 & 2 (Round to nearest 1mg)

- Mix in 250mL Normal Saline; Infuse over 2 hours

5-FLUOROURACIL 400 mg/m² IV Days 1 & 2 (Round to nearest 25mg)

- May give by slow push through sidearm of free flowing IV, immediately after Leucovorin

THEN

5-FLUOROURACIL 600mg/m² CIV for 22 hours Days 1 & 2

Start infusion immediately after each bolus injection of 5-Fluorouracil

- Continuous infusion using ambulatory infusion pump
- Infuse through central venous access device, if available
- Infuse through patent peripheral venous catheter, if infusion site used for only 3 days;

Inspect peripheral infusion sites daily and replace if evidence of irritation or extravasation

- Protect from light (Round to nearest 50mg- Max. 2g/day)

REPEAT EVERY 14 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic before chemotherapy
- May give Dopamine Receptor Antagonist PO before chemotherapy (Prochlorperazine 10mg PO or Metoclopramide 10-20mg PO)
- After chemotherapy, use Prochlorperazine 10 mg PO q4h PRN, or Metoclopramide 10 mg PO q4h PRN
- Patients **recommended** to suck on ice chips during bolus injection and for 30 minutes after, to reduce stomatitis

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth
- Baseline liver function tests (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated) & renal function tests [serum creatinine, electrolytes & BUN] (if severe organ failure suspected)
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$, or if Platelets = $< 100 \times 10^9/L$, notify physician and **REDUCE** 5FU to **50%** dose
2. If ANC $< 1.0 \times 10^9/L$ **OR** if Platelets $< 75 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Gastrointestinal Toxicities

1. If Mucositis or Diarrhea $\geq$ Grade 3 in previous course, **REDUCE** to **50%** dose

Hepatic dysfunction (*Suggested action*)

1. If bilirubin elevated above $85 \mu\text{mol/L}$ (marked hepatic dysfunction), **OMIT** dose

Cutaneous Toxicity

1. If clinical evidence of palmar-plantar erythematosis (hand-foot syndrome), **HOLD** dose until symptoms are resolved

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:

Days 1 & 2 = Approximately 2 1/2 -3 hours

Day 3 = 15 minutes

GI-FL-FU***CIV46**

5-Fluorouracil-Leucovorin/ 5-Fluorouracil 46 Hour Continuous Infusion (Simplified Bimonthly LV5FU2 Regimen- SBR)

(Advanced Colorectal Carcinoma)

BASIC LEVEL REGIMEN-

Community Hospital with
Oncology Nurses

LEUCOVORIN 400mg/m² IV Day 1 (Round to nearest 1mg)

- Mix in 250mL Normal Saline; Infuse over 2 hours

5-FLUOROURACIL 400 mg/m² IV Day 1 (Round to nearest 25mg)

- May give by slow push through sidearm of free flowing IV, immediately after Leucovorin

THEN

5-FLUOROURACIL 2400-3600mg/m² CIV for 46 hours Day 1

Start infusion immediately after bolus injection of 5-Fluorouracil

- Continuous infusion using ambulatory infusion pump
- Infuse through central venous access device, if available
- Infuse through patent peripheral venous catheter, if infusion site used for only 3 days; Inspect peripheral infusion sites daily and replace if evidence of irritation or extravasation
- Protect from light (Round to nearest 50mg)

REPEAT EVERY 14 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic before chemotherapy
- May give Dopamine Receptor Antagonist PO before chemotherapy (Prochlorperazine 10mg PO or Metoclopramide 10-20mg PO)
- After chemotherapy, use Prochlorperazine 10 mg PO q4h PRN, or Metoclopramide 10 mg PO q4h PRN
- Patients **recommended** to suck on ice chips during bolus injection and for 30 minutes after, to reduce stomatitis

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth
- Baseline liver function tests (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated) & renal function tests [serum creatinine, electrolytes & BUN] (if severe organ failure suspected)
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth
- Skin assessment, especially extremities

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GI-FL-FU*^{CIV46}

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, notify physician and **REDUCE** 5FU to **50%** dose
2. If ANC $< 1.0 \times 10^9/L$ **OR** if Platelets $< 75 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Gastrointestinal Toxicities

1. If Mucositis or Diarrhea $\geq$ Grade 3 in previous course, **REDUCE** to **50%** dose

Hepatic dysfunction (*Suggested action*)

1. If bilirubin elevated above $85 \mu\text{mol/L}$ (marked hepatic dysfunction), **OMIT** dose

Cutaneous Toxicity

1. If clinical evidence of palmar-plantar erythematosis (hand-foot syndrome), **HOLD** dose until symptoms are resolved

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT

Days 1 & 2 = Approximately 2 1/2 -3 hours

Day 3 = 15 minutes

GI

GI-FU-MITO

5-FLUOROURACIL Infusion/ Mitomycin Chemotherapy

(Combined Modality: Carcinoma of the
Anus)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

MITOMYCIN 10mg/m² IV on Day 1

(Round to nearest 0.25mg to a maximum of 20 mg))

- Slow push through sidearm of free flowing IV During WEEKS 1 & 5 of Radiotherapy

5-FLUOROURACIL 1000mg/m²/day CIV for 96 hours Start on Day 1

(Round to nearest 50mg- Max. 2g/day)

- Continuous infusion using ambulatory infusion pump
- Infuse through patent peripheral venous catheter; Inspect peripheral infusion sites daily and replace if evidence of irritation or extravasation

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

INTERMEDIATE RISK

Pre-Chemotherapy-

- Dexamethasone 8 mg PO, **AND**
- Dopamine Receptor Antagonist PO (Prochlorperazine 10mg PO, or Metoclopramide 10mg PO)

Post-Chemotherapy-

- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4h PRN or Metoclopramide 10 mg PO q3-4h)

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

DOSE MODIFICATION

Hematologic Toxicities:

1. If ANC < 1.5 x 10⁹/L, or if Platelets = <100 x 10⁹/L, notify physician and **REDUCE** 5FU to **50%** dose
2. If ANC < 1.0 x 10⁹/L **OR** if Platelets < 75 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Gastrointestinal Toxicities:

1. If Mucositis or Diarrhea ≥ Grade 3 in previous course, **REDUCE** to **50%** dose of 5-FU

Hepatic dysfunction

1. If Bili = 50-85μmol/L or AST > 180IU/L, **REDUCE** dose of Mitomycin to **75%** dose
2. If Bili above 85μmol/L, **STOP** both drugs

Renal failure (Suggested action)

1. If CrCl < 12mL/min, **REDUCE** dose of Mitomycin to **75%** dose

Continued Next Page...

GI-FU-MITO

CLINICAL MONITORING

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Baseline liver function tests** (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated) & **renal function tests** [serum creatinine, electrolytes & BUN]
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Skin assessment**, especially extremities
- **Local Site Toxicity** ratings, if incident of phlebitis
- **Neurological toxicity (Lethargy)** if patient complaint of symptoms

LETHARGY

0. None
1. Mild (Performance Status decreased by 1)
2. Moderate (Performance Status decreased by 2)
3. Severe (Performance Status decreased by 3)

LOCAL SITE TOXICITY

0. None
1. Pain
2. Pain & inflammation; phlebitis
3. Ulceration
4. Plastic surgery

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:

Day 1 = 1 hour

Days 2 to 5 = 15 to 30 minutes

GI-GEMCIT

Gemcitabine Chemotherapy

(Advanced or Unresectable
Pancreatic Carcinoma)

BASIC LEVEL REGIMEN-

Community Hospital with Oncology
Nurses

GEMCITABINE 1000 mg/m² IV Days 1, 8 & 15

May give dose on Day 22 in Cycle 1 ONLY (Round to nearest 20mg)
(Dosing schedule may be adjusted for myelosuppression in each patient)

- Mix drug in 250mL bag (Normal Saline); Infuse over 30 minutes through free-flowing IV

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic before chemotherapy
- May give Dopamine Receptor Antagonist PO before chemotherapy (Prochlorperazine 10mg PO or Metoclopramide 10-20mg PO)

DOSE MODIFICATION

Hematologic Toxicities:

1. If ANC = $0.5-1.0 \times 10^9/L$, OR if Platelets = $50-100 \times 10^9/L$, notify physician and **REDUCE** to 75% dose
2. If ANC < $0.5 \times 10^9/L$ OR if Platelets < $50 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Baseline and regular liver function tests [serum alkaline phosphatase, GGT, AST, ALT & Bilirubin levels] and renal function tests [serum creatinine, electrolytes & BUN]
- Baseline and routine renal function tests [serum creatinine, serum electrolytes] before each treatment cycle
- Check for edema at each visit
- Routine toxicity ratings of Flu-like Symptoms, Lethargy at each visit

LETHARGY

0. None
1. Mild (Performance Status [PS] decreased by 1)
2. Moderate (PS decreased by 2)
3. Severe (PS decreased by 3)

FLU-LIKE SYMPTOMS

(Arthralgia, myalgia, diaphoresis, rigours/chills)

0. None
1. Mild
2. Moderate
3. Severe

Rated at each clinic visit

EDEMA

0. None
1. 1+ or dependant evening only
2. 2+ or dependant throughout the day
3. 3+
4. 4+, generalized anasarca

Rated if Edema noted on routine visits

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:
Approx. 45 minutes

[Rev. 05/01]]

GI-IRINO*W

Low Dose Weekly Irinotecan Chemotherapy

(Metastatic Colorectal Carcinoma)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

IRINOTECAN 125mg/m² IV Days 1, 8, 15 & 22 (Round to nearest 1mg)

- Mix in 500mL bag (5% Dextrose); Infuse over 90 minutes

Dose Level	0	-1	-2	-3
Irinotecan(mg/m ²)	125	100	75	50

For Acute Cholinergic Syndrome- ATROPINE 0.25mg SC be given to prevent cholinergic adverse effects or within 1 hour post-chemo for acute-onset diarrhea

LOPERAMIDE 4mg PO at the onset of diarrhea (or ANY change in bowel movements), then 2mg q2h PO until patient is diarrhea-free (or bowel movements have returned to normal) for 12 hours (May take 4mg q4h at night for convenience)

- Ensure patient has adequate supply of Loperamide at home (dispense with first cycle, then as needed), and is instructed on when & how to use the medication

REPEAT EVERY 42 DAYS- 28 DAYS OF TREATMENT, THEN REST PERIOD FOR 2 WEEKS BETWEEN CYCLES

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: INTERMEDIATE RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100mg PO/IV), **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO/IV)

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4h PRN, or Metoclopramide 10mgPO q4h PRN
- **AVOID** Prochlorperazine on the day(s) Irinotecan is administered

GUIDELINE

See the CCNS website
www.cancercare.ns.ca for the
guideline for Irinotecan for Colorectal
cancer

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

Continued Next Page...

GI-IRINO*W

CLINICAL MONITORING

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each day of treatment
- **Performance Status** measured at each visit
- **Baseline and regular liver function tests** [serum alkaline phosphatase, GGT, AST, ALT & Bilirubin levels]
- **Routine assessment of Diarrhea**, at each clinic visit (Days 1, 8, 15 & 22) and telephone reinforcement

DIARRHEA

0. None

1. Increase of 2-3 stools/day over pretreatment
2. Increase of 4-6 stools/day or nocturnal stools
3. Increase of 7-9 stools/day, incontinence, malabsorption
4. Increase of ≥ 10 stools/day, grossly bloody diarrhea, need for parenteral nutrition support

Rated at each visit and between visits by telephone assessment

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$, notify physician and **REDUCE** Irinotecan by one dose level ($25\text{mg}/\text{m}^2$)
2. If ANC $< 1.0 \times 10^9/L$, notify physician and **HOLD** dose for 1 week (or until ANC ≥ 1.5), then restart at dose reduced by one dose level ($25\text{mg}/\text{m}^2$)
3. If ANC $< 0.5 \times 10^9/L$, notify physician and **HOLD** dose for 1 week (or until ANC ≥ 1.5), then restart at dose reduced by two dose levels ($50\text{mg}/\text{m}^2$)

Gastrointestinal Toxicities

1. If Diarrhea = Grade 2, **REDUCE** Irinotecan by $25\text{mg}/\text{m}^2$
2. If Diarrhea = Grade 3, **HOLD** until $\leq$ grade 2, then restart at dose reduced by $25\text{mg}/\text{m}^2$
3. If Diarrhea = Grade 4, **HOLD** until $\leq$ grade 2, then restart at dose reduced by $50\text{mg}/\text{m}^2$

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT

Approximately 2 hours

GI-IRINO*3W

High Dose 3-Weekly Irinotecan Chemotherapy

(Metastatic Colorectal Carcinoma)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

IRINOTECAN 350mg/m² IV Day 1 (Round to nearest 1mg)

- Mix in 500mL bag (5% Dextrose). Infuse over 90 minutes
- Reduce dose to lower dose level if rectal Radiotherapy is given

Dose Level	0	-1	-2	-3
Irinotecan(mg/m ²)	350	300	250	200

For Acute Cholinergic Syndrome- ATROPINE 0.25mg SC be given to prevent cholinergic adverse effects or within 1 hour post-chemo for acute-onset diarrhea

LOPERAMIDE 4mg PO at the onset of diarrhea (or ANY change in bowel movements), then 2mg q2h PO until patient is diarrhea-free (or bowel movements have returned to normal) for 12 hours (May take 4mg q4h at night for convenience)

- Ensure patient has adequate supply of Loperamide at home (dispense with first cycle, then as needed), and is instructed on when & how to use the medication

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: INTERMEDIATE RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100mg PO/IV), **AND**

- Dexamethasone 8mg PO (may increase to 20mg PO/IV)

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4h PRN, or Metoclopramide 10mg PO q4h PRN
- **AVOID** Prochlorperazine on the day(s) Irinotecan is administered

GUIDELINE

See the CCNS website
www.cancercarens.ca for the
guideline for Irinotecan for Colorectal
cancer

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

GI-IRINO*3W

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each day of treatment
- Performance Status measured at each visit
- Baseline and regular liver function tests [serum alkaline phosphatase, GGT, AST, ALT & Bilirubin levels]
- Routine assessment of Diarrhea at each clinic visit (Days 1, 8, 15 & 22) and telephone reinforcement

DIARRHEA

0 None

- 1 Increase of 2-3 stools/day over pretreatment
- 2 Increase of 4-6 stools/day or nocturnal stools
- 3 Increase of 7-9 stools/day, incontinence, malabsorption
- 4 Increase of ≥ 10 stools/day, grossly bloody diarrhea, need for parenteral nutrition support

Rated at each visit and between visits by telephone assessment

DOSE MODIFICATION

Hematologic Toxicities

- 1 If ANC $< 1.5 \times 10^9/L$, notify physician and **REDUCE** Irinotecan by one dose level (25mg/m²)
- 2 If ANC $< 1.0 \times 10^9/L$, notify physician and **HOLD** dose for 1 week (or until ANC ≥ 1.5), then restart at dose reduced by one dose level (25mg/m²)
- 3 If ANC $< 0.5 \times 10^9/L$, notify physician and **HOLD** dose for 1 week (or until ANC ≥ 1.5), then restart at dose reduced by two dose levels (50mg/m²)

Gastrointestinal Toxicities

- 1 If Diarrhea = Grade 2, **REDUCE** Irinotecan by 25mg/m²
- 2 If Diarrhea = Grade 3, **HOLD** until $\leq$ grade 2, then restart at dose reduced by 25mg/m²
- 3 If Diarrhea = Grade 4, **HOLD** until $\leq$ grade 2, then restart at dose reduced by 50mg/m²

NOTE

Similar outcomes to GI-IRINO*W, but higher drug costs for chemotherapy

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT

Approximately 2 hours

GI-IFL

Irinotecan-Bolus Fluorouracil-Leucovorin (Saltz) Chemotherapy

(Metastatic Colorectal Carcinoma-1st Line Treatment)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated Cancer Treatment Unit

BASIC LEVEL REGIMEN- (5FU-Leucovorin ONLY) Community Hospital with Oncology Nurses

IRINOTECAN 125mg/m² IV Days 1, 8, 15 & 22 (Round to nearest 1mg)

- Mix in 500mL bag (5% Dextrose); Infuse over 90 minutes
- May give first dose at Dose Level -1, then increase to Dose Level 0 if no toxicity.

If toxic reaction, may further reduce dose level.

Dose Level	0	-1	-2	-3
Irinotecan(mg/m ²)	125	100	75	50
5-Fluorouracil(mg/m ²)	500	400	300	200

For Acute Cholinergic Syndrome- ATROPINE 0.25mg SC be given to prevent cholinergic adverse effects or within 1 hour post-chemo for acute-onset diarrhea

LEUCOVORIN 20mg/m² IV Days 1, 8, 15 & 22 (Round to nearest 1mg)

- Inject by direct IV push, followed by a Normal Saline flush, if no IV line has been set up
- May give by slow push through sidearm of free flowing IV
- The injection must not exceed 160mg/min of leucovorin (due to calcium content)

5-FLUOROURACIL 500mg/m² IV Days 1, 8, 15 & 22
(Round to nearest 25mg)

- Inject by direct IV push, followed by a Normal Saline flush, if no IV line has been set up
- May give by slow push through sidearm of free flowing IV

LOPERAMIDE 4mg PO at the onset of diarrhea (or ANY change in bowel movements), then 2mg q2h PO until patient is diarrhea-free (or bowel movements have returned to normal) for 12 hours (May take 4mg q4h at night for convenience)

- Ensure patient has adequate supply of Loperamide at home (dispense with first cycle, then as needed), and is instructed on when & how to use the medication

REPEAT EVERY 42 DAYS- 28 DAYS OF TREATMENT, THEN REST PERIOD FOR 2 WEEKS BETWEEN CYCLES

GUIDELINE

See the CCNS website
www.cancercarens.ca for the
guideline for Irinotecan for Colorectal
cancer

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

SUPPORTIVE CARE

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV). **AND**
- Dexamethasone 8mg PO (may increase to 20mgPO/IV)

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4h PRN, or Metoclopramide 10mgPO q4h PRN)
- **AVOID** Prochlorperazine on the day(s) Irinotecan is administered
- Patients **recommended** to suck on ice chips during bolus 5Fluorouracil injections, to reduce stomatitis

NOTE

- Severe cholinergic and symptomatic reactions have been noted in patients on the IFL regimen. Follow patients closely and (in the first week) with daily or alternate day discussions/phone calls, to identify drug toxicity early. Return appointments will be booked for week 3, to follow up for any signs of toxicity.
- Toxicity may be exaggerated from normal expectations and will require prompt attention. Patient deaths have been recorded from drug-related toxicity on the IFL regimen
- Also known as Saltz Regimen

GI-IFL

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each day of treatment
- **Performance Status** measured at each visit
- Baseline and regular **liver function tests** [serum alkaline phosphatase, GGT, AST, ALT & Bilirubin levels]
- **Clinical assessment of stomatitis**, oral examination upon patient complaint of a sore mouth
- Routine assessment of Diarrhea, at each clinic visit (Days 1, 8, 15 & 22) and telephone reinforcement

DIARRHEA

- 0 None
- 1 Increase of 2-3 stools/day over pretreatment
- 2 Increase of 4-6 stools/day or nocturnal stools
- 3 Increase of 7-9 stools/day, incontinence, malabsorption
- 4 Increase of ≥ 10 stools/day, grossly bloody diarrhea, need for parenteral nutrition support

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$ or if Platelets = $75-100 \times 10^9/L$, notify physician and **REDUCE** Irinotecan and 5FU by one dose level ($25\text{mg}/\text{m}^2$ of Irinotecan and $100\text{mg}/\text{m}^2$ of 5FU)
2. If ANC $< 1.0 \times 10^9/L$ **OR** if Platelets $< 75 \times 10^9/L$, notify physician and **HOLD** dose for 1 week (or until ANC ≥ 1.5), then restart Irinotecan and 5FU at dose reduced by one dose level
3. If ANC $< 0.5 \times 10^9/L$, notify physician and **HOLD** dose for 1 week (or until ANC ≥ 1.5), then restart Irinotecan and 5FU at dose reduced by two dose levels ($50\text{mg}/\text{m}^2$ of Irinotecan and $200\text{mg}/\text{m}^2$ of 5FU)

Gastrointestinal Toxicities

1. If Diarrhea = Grade 2, notify physician and **REDUCE** by one dose level
2. If Diarrhea = Grade 3, notify physician & **HOLD** until $\leq$ grade 2, then restart at dose reduced by one dose level
3. If Diarrhea = Grade 4, notify physician and **HOLD** until $\leq$ grade 2, then restart at dose reduced by two dose levels

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT

Approximately 2 hours

GI-IFL*SBR

**Irinotecan-Fluorouracil-
Leucovorin (FOLFIRI)
Chemotherapy**

(Metastatic Colorectal Carcinoma-
1st Line Treatment)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

**BASIC LEVEL REGIMEN- (5FU-
Infusion Management ONLY)**
Community Hospital with
Oncology Nurses

IRINOTECAN 180mg/m² IV Day 1 (Round to nearest 1mg)

- Mix in 500mL bag (5% Dextrose); Infuse over 90 minutes
- May give first dose at Dose Level -1, then increase to Dose Level 0 if no toxicity. If toxic reaction, may further reduce dose level.

Dose Level	+1	0	-1	-2
Irinotecan(mg/m ²)	180	180	150	120
5-Fluorouracil Bolus(mg/m ²)	400	400	320	240
5-Fluorouracil Infusion (mg/m ²)	3000	2400	2000	1600

For Acute Cholinergic Syndrome- ATROPINE 0.25mg SC be given to prevent cholinergic adverse effects or within 1 hour post-chemo for acute-onset diarrhea

LEUCOVORIN 400mg/m² IV Day 1 (Round to nearest 1mg)

- Mix in 250mL Normal Saline; Infuse over 2 hours

5-FLUOROURACIL 400 mg/m² IV Day 1 (Round to nearest 25mg)

- May give by slow push through sidearm of free flowing IV, immediately after Leucovorin

THEN

5-FLUOROURACIL 2400mg/m² CIV for 46 hours Day 1

Start infusion immediately after bolus injection of 5-Fluorouracil

- Continuous infusion using ambulatory infusion pump; start after 5-Fluorouracil Bolus IV dose
- Infuse through central venous access device, if available
- Infuse through patent peripheral venous catheter, if infusion site used for no more than 3 days; inspect peripheral site daily and replace if evidence of irritation or extravasation

LOPERAMIDE 4mg PO at the onset of diarrhea (or ANY change in bowel movements), then 2mg q2h PO until patient is diarrhea-free (or bowel movements have returned to normal) for 12 hours (May take 4mg q4h at night for convenience)

- Ensure patient has adequate supply of Loperamide at home (dispense with first cycle, then as needed), and is instructed on when & how to use the medication

REPEAT EVERY 14 DAYS

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

Continued Next Page...

GI-IFL*SBR

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: INTERMEDIATE RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo,
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4h PRN, or Metoclopramide 10mgPO q4h PRN)
- **AVOID** Prochlorperazine on the day(s) Irinotecan is administered
- Patients **recommended** to suck on ice chips during bolus 5Fluorouracil injections, to reduce stomatitis

NOTE

- Severe cholinergic and symptomatic reactions have been noted in patients on the IFL regimen. Follow patients closely and (in the first week) with daily or alternate day discussions/phone calls, to identify drug toxicity early. Return appointments will be booked for week 2, to follow up for any signs of toxicity.
- Toxicity may be exaggerated from normal expectations and will require prompt attention. Patient deaths have been recorded from drug-related toxicity on the IFL regimen.
- Also known as FOLFIRI 1 regimen

GUIDELINE

See the CCNS website www.cancercare.ns.ca for the guideline for Irinotecan for Colorectal cancer

GI-IFL***SBR**

CLINICAL MONITORING

- **Complete blood count** including differential, platelets and hemoglobin (CBC) before each day of treatment
- **Performance Status** measured at each visit
- Baseline and regular **liver function tests** [serum alkaline phosphatase, GGT, AST, ALT & Bilirubin levels]
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- Routine assessment of Diarrhea, at each clinic visit (Days 1, 8, 15 & 22) and telephone reinforcement

DIARRHEA

0. None

1. Increase of 2-3 stools/day over pretreatment
2. Increase of 4-6 stools/day or nocturnal stools
3. Increase of 7-9 stools/day, incontinence, malabsorption
4. Increase of ≥ 10 stools/day, grossly bloody diarrhea, need for parenteral nutrition support

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$ or if Platelets = $75-100 \times 10^9/L$, notify physician and **REDUCE** Irinotecan + 5FU by one dose level
2. If ANC $< 1.0 \times 10^9/L$ **OR** if Platelets $< 75 \times 10^9/L$, notify physician and **HOLD** dose for 1 week (or until ANC ≥ 1.5), then restart Irinotecan + 5FU at dose reduced by one dose level
3. If ANC $< 0.5 \times 10^9/L$, notify physician and **HOLD** dose for 1 week (or until ANC ≥ 1.5), then restart Irinotecan + 5FU at dose reduced by 2 dose levels

Gastrointestinal Toxicities

1. If Diarrhea = Grade 2, **REDUCE** by one dose level
2. If Diarrhea = Grade 3, **HOLD** until $<$ grade 2, then restart at dose reduced by one dose level
3. If Diarrhea = Grade 4, **HOLD** until $<$ grade 2, then restart at dose reduced by two dose levels
4. If Mucositis or Diarrhea $>$ Grade 3 in previous course, **REDUCE** 5FU and Leucovorin dose

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT

Approximately 4 hours

GI-OFL***SBR**

Oxaliplatin-Fluorouracil- Leucovorin (SBR) Chemotherapy

(Metastatic Colorectal Carcinoma-
1st Line Treatment)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

OXALIPLATIN 100mg/m² IV Day 1

- Mix in 250mL minibag (5% Dextrose); Infuse over 2 hours
- Increase infusion to 6 hours if symptoms of pharyngolaryngeal dysesthesia
- Administer at the same time as Leucovorin but BEFORE 5-Fluorouracil; flush line thoroughly with 5% Dextrose solution before 5-Fluorouracil administered

LEUCOVORIN 400mg/m² IV Day 1 (Round to nearest 1mg)

- Mix in 250 mL 5% Dextrose solution (NOT Normal Saline); Infuse through Y-site connection over 2 hours concurrently with Oxaliplatin, before 5-Fluorouracil injection

5-FLUOROURACIL 400 mg/m² IV Day 1 (Round to nearest 25mg)

- May give by slow push through sidearm of free flowing IV, immediately after Leucovorin

THEN

5-FLUOROURACIL 2400-3000mg/m² CIV for 46 hours Day 1

Start infusion immediately after bolus injection of 5-Fluorouracil

- Continuous infusion using ambulatory infusion pump; start after 5-Fluorouracil Bolus IV dose
- Infuse through central venous access device, if available
- Infuse through patent peripheral venous catheter, if infusion site used for no more than 3 days; inspect peripheral site daily and replace if evidence of irritation or extravasation

REPEAT EVERY 14 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: INTERMEDIATE RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist IV (Ondansetron 8mg IV q12h on Day 1, **OR** Granisetron 1mg IV, **OR** Dolasetron 100mg IV), **AND**
- Dexamethasone 20mg IV

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 days, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo,
- Dopamine Receptor Antagonist (Metoclopramide 10mg PO PRN; **OR** Prochlorperazine 10mg PO/PR PRN)
- Patients **are NOT recommended** to suck on ice chips during bolus injection

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CLINICAL MONITORING

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each day of treatment
 - **Performance Status** measured at each visit
 - **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
 - **Baseline liver function tests** (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated) & **renal function tests** [serum creatinine, electrolytes & BUN] (if severe organ failure suspected)
 - **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
 - **Skin assessment**, especially extremities
 - Monitoring for **symptoms of Pharyngolaryngo- dysesthesia** at each visit, toxicity ratings to track experience
 - **Neurologic (Sensory)** ratings at each visit
- PHARYNGOLARYNGODYSESTHESIA**
- 0. No change
 - 1. Paraesthesia/dysesthsias (P/D) of short duration that resolve and do not interfere with function (may be cold-induced)
 - 2. P/D interfering with function but not activities of daily living (ADL)
 - 3. P/D with pain or functional impairment that also interfere with ADL
 - 4. Persistent P/D that are disabling or life-threatening
- SENSORY**
- 0. No change
 - 1. Mild paraesthesia; no deep tendon reflex
 - 2. Mild/moderate sensory loss; moderate paraesthesia
 - 3. Sensory loss interferes with function

Rated At Each Clinic Visit

GI-OFL*SBR

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$ or if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week (or until ANC ≥ 1.5)

Neurotoxicity

1. If troublesome but no functional impairment for >7 days (or until next cycle), **REDUCE** dose from $130\text{mg}/\text{m}^2$ to $100\text{mg}/\text{m}^2$ or from $85\text{mg}/\text{m}^2$ to $65\text{mg}/\text{m}^2$, or from $65\text{mg}/\text{m}^2$ to $50\text{mg}/\text{m}^2$
2. If functional impairment for >7 days, **REDUCE** dose from $85\text{mg}/\text{m}^2$ to $50\text{mg}/\text{m}^2$
3. If functional impairment persists to next cycle, **DISCONTINUE** Oxaliplatin (may resume therapy if neurotoxicity improves or resolves)

NOTES

- Oxaliplatin is only available through physician letter of request to the Special Access Program, Health Canada. This is also a non-formulary drug, and requires authorization of the Cancer Care program administration, on a case-by-case basis. Until the drug is licenced in Canada, and approved for the hospital formulary, **this regimen is NOT recommended for routine use.**
- Also known as FOLFOX 6 regimen

GUIDELINE

See the CCNS website www.cancercare.ns.ca for the guideline for Oxaliplatin for Colorectal cancer

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT

Approximately 4 hours

GI-OXALI

Oxaliplatin Chemotherapy

(Advanced Colorectal Carcinoma-
Salvage Treatment- Palliative Intent)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

OXALIPLATIN 130mg/m² IV Day 1

REPEAT EVERY 21 DAYS

OR: **85-100mg/m² IV Day 1- REPEAT EVERY 21 DAYS**

- Mix in 250mL minibag (5% Dextrose- **NOT** Normal Saline); Infuse over 2 hours
- Increase infusion to 6 hours if symptoms of pharyngolaryngeal dysesthesia

SUPPORTIVE CARE

ANTIEMETIC REGIMEN HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist IV (Ondansetron 8mg IV q12h on Day 1, **OR** Granisetron 1mg IV, **OR** Dolasetron 100mg IV), **AND**
- Dexamethasone 20mg IV

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 days, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
- Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Dopamine Receptor Antagonist (Metoclopramide 10mg PO PRN, **OR** Prochlorperazine 10mg PO/PR PRN)
- **Patients are NOT recommended to suck on ice chips during bolus injection**

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week (or until ANC ≥ 1.5)

Neurotoxicity

1. If troublesome but no functional impairment for >7 days (or until next cycle), **REDUCE** dose from 130mg/m² to 100mg/m² or from 85mg/m² to 65mg/m², or from 65mg/m² to 50mg/m²
2. If functional impairment for >7 days, **REDUCE** dose from 85mg/m² to 50mg/m²
3. If functional impairment persists to next cycle, **DISCONTINUE** Oxaliplatin (may resume therapy if neurotoxicity improves or resolves)

NOTE

Oxaliplatin is only available through physician letter of request to the Special Access Program, Health Canada. This is also a non-formulary drug, and requires authorization of the Cancer Care program administration, on a case-by-case basis. Until the drug is licenced in Canada, and approved for the hospital formulary, **this regimen is NOT recommended for routine use.**

GI-OXALI

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Monitoring for **symptoms of Pharyngolaryngo- dysesthesia** at each visit, toxicity ratings to track experience
- **Neurologic** (Sensory) ratings at each visit
PHARYNGOLARYNGODYSESTHESIA
- 0. No change
- 1. Paraesthesia/dysesthsias (P/D) of short duration that resolve and do not interfere with function (may be cold-induced)
- 2. P/D interfering with function but not activities of daily living (ADL)
- 3. P/D with pain or functional impairment that also interfere with ADL
- 4. Persistent P/D that are disabling or life-threatening
SENSORY
- 0. No change
- 1. Mild paraesthesia; no deep tendon reflex
- 2. Mild/moderate sensory loss; moderate paraesthesia
- 3. Sensory loss interferes with function

Rated At Each Clinic Visit

GUIDELINE

See the CCNS website
www.cancercare.ns.ca for the
guideline for Oxaliplatin for Colorectal
cancer

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:
Approximately 2-3 hours

GI

GI-RALT1

Raltitrexed Chemotherapy

(Advanced Colorectal Carcinoma-
Palliative Intent)

BASIC LEVEL REGIMEN-
Community Hospital with Oncology
Nurses

RALTITREXED 3mg/m² IV Day 1 (Round to nearest 1mg)

• Mix in 100mL minibag (5% Dextrose); Infuse over 15 minutes

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic before chemotherapy
- May give Dopamine Receptor Antagonist PO before chemotherapy (Prochlorperazine 10mg PO or Metoclopramide 10-20mg PO)
- After chemotherapy, use Prochlorperazine 10 mg PO q4h PRN, or Metoclopramide 10 mg PO q4h PRN
- *Patients recommended to suck on ice chips during Raltitrexed injections, to reduce stomatitis*

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Baseline & regular renal function tests [serum creatinine, electrolytes & BUN]
- Baseline & regular liver function tests (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated)
- Clinical assessment of stomatitis, oral examination upon patient complaint of a sore mouth

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets = 75-100 x 10⁹/L, notify physician and **REDUCE** to 50% dose
2. If ANC < 1.0 x 10⁹/L OR if Platelets < 75 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Gastrointestinal Toxicities

1. If Grade 2 diarrhea or stomatitis, **reduce** to 75% dose
2. If Grade 3 diarrhea or stomatitis, **reduce** to 50% dose
3. If Grade 3 diarrhea with severe neutropenia (<0.5 x 10⁹/L) or thrombocytopenia (<10 x 10⁹/L), **OMIT** dose
4. If Grade 4 diarrhea or stomatitis, **OMIT** dose

Renal failure (Suggested action)

1. If CrCl 55-65 mL/min, **reduce** Raltitrexed to 75% dose, and give every 28 days
2. If CrCl = 25-54 mL/min, **reduce** Raltitrexed to 25-54% dose (%age equivalent to CrCl), and give every 28 days
3. If CrCl <25mL/min, **stop** Raltitrexed

Hepatic Failure (Suggested action)

1. If pre-existing hyperbilirubinemia, no dosage change
2. If bilirubin increase suspected to be related to drug, delay dosage until resolved

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

Continued Next Page

GI-RALT**NOTE**

- Substitution of Raltitrexed for Fluorouracil-Leucovorin must be made with caution. Some studies have shown significantly higher treatment-related mortality with Raltitrexed, with equivalent overall survival between the two arms. Treatment-related mortality was associated with undetected renal dysfunction. This regimen is **NOT** recommended for routine use.
- *TomudexTM* is the brand name for Raltitrexed.

PATIENT VISIT**CHEMOTHERAPY PATIENT VISIT**

Approximately 15 minutes

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NOTE: Regimen names in *italics* are not in this pocketbook version. See full version for regimen monograph.

GU-BCG

BCG (Bacille Calmette-Guerin) Instillation

(Bladder Carcinoma- Curative Intent)

BASIC LEVEL REGIMEN-
Community Hospital with
Oncology Nurses, OR

Take-Home Prescription-
Physician Office Administration

BCG (Bacille Calmette-Guerin) INTRAVESICULAR INSTILLATION

Dosing varies by specific products:

- OncoTICE™ 1 ampul diluted to 30-50 mL Instil weekly for 6 weeks, then on weeks 8 & 12, then monthly for months 4 to 12 (1 to 8×10^8 CFU/ampul - Organon brand)
- ImmuCyst™ 1 ampul diluted to 30-50mL Instil weekly for 6 weeks, then at 3, 6, 12, 18, & 24 months (81 mg/ampul - Connaught brand)
- PACIS™ 1 ampul or vial diluted to 30-50mL Instil weekly for 6 weeks, then at 3, 6, 12, 18, & 24 months (120 mg/ampul or vial, BioChem Vaccines)

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: NOT APPLICABLE

- If there are bladder spasms, a B&O suppository may be used PRN

CLINICAL MONITORING

- Watch for signs of urinary infection, especially with prolonged cystitis, hematuria, signs of systemic tuberculosis infections

DOSE MODIFICATION

Hematologic Toxicities

1. If WBC $< 3.0 \times 10^3$ /L, notify physician and **HOLD** dose for 1 week

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT
Approx. 1 1/2 hours/day

GU

GU-BEP

CISPLATIN-ETOPOSIDE- BLEOMYCIN (PEB) Chemotherapy

(Testicular Cancer)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

PREHYDRATION

- Encourage patients to drink 6-8 glasses of water prior to chemo each day (increase fluids if poorly hydrated)

- May prehydrate with 1000mL Normal Saline; Infuse over 60 minutes

ETOPOSIDE 100mg/m² IV daily Days 1 to 5 (Round to nearest 10mg)

- Premixed in 1000mL bags of Normal Saline; Infuse over 60 minutes

- Give Etoposide BEFORE Cisplatin, to hydrate patient

CISPLATIN 20mg/m² IV daily Days 1 to 5 (Round to nearest 1mg)

- Mix drug in 250mL bag (Normal Saline); Infuse over 60 minutes

- May also admix 20G Mannitol (200mL of 10% solution) with Cisplatin

BLEOMYCIN 30mg IV Days 2, 9 & 16

- Mix drug in 100mL bag (Normal Saline); Infuse over 15 minutes

- May give 1mg test dose before first treatment, observe for 30 minutes, then administer balance of dose if no reaction

- May give Diphenhydramine 25mg IV or Hydrocortisone 100mg IV before Bleomycin to prevent hypersensitivity reaction

POSTHYDRATION

- May give 1000mL Normal Saline if additional hydration needed; May add 10mEq/L KCl and 8mmol/L MgSO₄ to Normal Saline; Infuse over 60 minutes

REPEAT EVERY 21 DAYS For a Total of 3 to 4 Cycles

NOTE

Since this is first-line therapy for a cancer which may be cured for life, it is important to pay close attention to short-term treatment-related toxicities, to avoid possible long-term adverse effects. Aggressive hydration is recommended to prevent sub-clinical nephrotoxicity.

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L OR if Platelets < 100 x 10⁹/L on Day 1, notify physician and **HOLD** doses for 1 week

Renal failure (Recommended actions)

1. If CrCl < 30mL/min or SerCr > 185µmol/L, consider substituting Carboplatin for Cisplatin dose
2. If CrCl = 12-48mL/min, **REDUCE** Bleomycin to **75%** dose
3. If CrCl < 12mL/min, **REDUCE** Bleomycin to **50%** dose

Continued Next Page...

GU-BEP

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: Days 1-5 - HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist prechemo each day (Ondansetron 8mg PO pre-chemo & 8mg PO qhs on Days 1 to 5; OR Granisetron 2mg PO prechemo each day; OR Dolasetron 100mg PO)- If patient has vomited on previous dose may give IV prechemo doses (Ondansetron 8mg IV; OR Granisetron 1mg IV; OR Dolasetron 100mg IV). **AND**
- Dexamethasone 8mg PO prechemo each day on Days 1 to 5- If patient has vomited on previous dose may give 8mg IV prechemo doses, or may increase Dexamethasone to 20mg PO/IV

Post-Chemotherapy-

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses after last chemo treatment, if given prechemo) **OR**
- No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
- Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo. **AND**
- Dexamethasone 8mg PO q24h for 3 doses after last chemo treatment

Bleomycin ONLY days -LOW RISK

- After chemotherapy, may use a Dopamine Receptor Antagonist PRN (Metoclopramide 10mg PO q4h PRN or Prochlorperazine 10mg PO/PR q4h PRN)

HYPERSENSITIVITY PROPHYLAXIS:

- May give Diphenhydramine 25mg IV and/or Hydrocortisone 100mg IV before Bleomycin dose

HYPERSENSITIVITY REACTION:

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

GU

Continued Next Page...

GU-BEP

CLINICAL MONITORING

- **Complete blood count** including differential, platelets and hemoglobin (CBC) and **serum electrolytes** (including Mg^{++}) before each cycle of treatment
- **Renal function tests** at baseline and before Day 1 of each cycle [measured creatinine clearance, serum creatinine, serum electrolytes (including magnesium, calcium, potassium levels) & BUN]
- **Liver function tests** at baseline and before Day 1 of each cycle [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]
- Tumour markers assessed at each cycle (AFP, β -hCG)
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Clinical pulmonary exam** at each visit, including pulmonary function tests, auscultation, pulmonary toxicity ratings (Cough, SOB)
- **Neurologic** toxicity ratings (Sensory) at each visit
- Baseline & periodic Hearing ratings, **hearing tests** if symptomatic

HEARING

- 0 No change
- 1 Asymptomatic
- 2 Tinnitus
- 1. Correctable hearing loss
- 2. Deafness

SENSORY

- 0 No change
- 1. Mild paraesthesia, no deep tendon reflex
- 2 Mild/moderate sensory loss; moderate paraesthesia
- 3 Sensory loss interferes with function

Rated at each clinic visit

COUGH

- 0. None
- 1 Mild
- 2. Moderate
- 3. Severe

SHORT OF BREATH

- 0. No change
- 1. Mild SOB
- 2. Dyspnea on exertion
- 3. Dyspnea at normal level of activity
- 4. Dyspnea at rest

Rated at each clinic visit, if Bleomycin dosage needs adjustment

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

PATIENT VISIT

CHEMOTHERAPY PATIENT VISITS:
Days 1 to 5: Approx. 3 hrs/day
Bleomycin Days: Approx. 30 min

GU-CISP-GEM

CISPLATIN-GEMCITABINE

Chemotherapy

(Advanced Bladder Carcinoma-
Palliative Intent)

INTERMEDIATE LEVEL REGIMEN-

Regional Hospital with Dedicated

Cancer Treatment Unit

BASIC LEVEL REGIMEN-

Gemcitabine ONLY days

GEMCITABINE 1000mg/m² IV Days 1, 8 and 15

(Dosing schedule may be adjusted for myelosuppression in each patient)

(Round to nearest 20mg)

- Mix drug in 250mL bag (Normal Saline); Infuse over 30 minutes through free-flowing IV

PREHYDRATION on Day 1

- Encourage patients to drink 6-8 glasses of water prior to chemo and on Days 1 & 2
(increase fluids if poorly hydrated)
- May give Normal Saline 1000mL; Infuse over 1 hour.
- May give 200mL of 10% Mannitol solution (20G); Infuse through sidearm over last 30 minutes before Cisplatin

CISPLATIN 70mg/m² IV Day 1 (Round to nearest 1mg)

- Mix drug in 500mL bag (Normal Saline); Infuse over 60 minutes

POSTHYDRATION on Day 1

- Normal Saline 1000mL; infuse over 1 hour
- May add 10mEq/L KCl and 8 mmol/L MgSO₄ to Normal Saline

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK-Day 1

Pre-Chemotherapy-

- Serotonin Receptor Antagonist IV (Ondansetron 8mg IV, OR Granisetron 1mg IV, OR Dolasetron 100mg IV), **AND**
- Dexamethasone 20mg IV PO **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *When available in Canada*

INTERMEDIATE RISK - Days 8 & 15

- Dopamine Receptor Antagonist PO Pre-Chemotherapy & PRN Post-Chemotherapy (Prochlorperazine 10mg PO q4h PRN; OR Metoclopramide 10mg PO q4h PRN)
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration (to prevent renal toxicity)

Continued Next Page...

GU-CISP-GEM

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes (including Mg^{++}) before each cycle of treatment
- Measured creatinine clearance before first cycle of chemotherapy
- Baseline and routine renal function tests [serum creatinine, serum electrolytes (including magnesium, calcium, potassium levels) & BUN] before Day 1 of each cycle of treatment
- Liver function [Bilirubin levels] checked at baseline and before each cycle of treatment
- Clinical assessment of stomatitis, oral examination upon patient complaint of a sore mouth
- Check for edema at each visit
- Routine toxicity ratings of Flu-like Symptoms, Lethargy at each visit
- Neurologic toxicity ratings (Sensory) at each visit
- Baseline & periodic Hearing ratings; hearing tests if symptomatic

HEARING

0. No change
1. Asymptomatic
2. Tinnitus
3. Correctable hearing loss
4. Deafness

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss, moderate paraesthesia
3. Sensory loss interferes with function

LETHARGY

0. None
1. Mild (Performance Status decreased by 1)
2. Moderate (Performance Status decreased by 2)
3. Severe (Performance Status decreased by 3)

FLU-LIKE SYMPTOMS

(Arthralgia, myalgia, diaphoresis, rigours/chills)

0. None
1. Mild
2. Moderate
3. Severe

Rated at each clinic visit

DOSE MODIFICATION

Hematologic Toxicities

1. On Day 1, if $ANC < 1.5 \times 10^9/L$ OR if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week
2. On days 8 or 15, if $ANC = 0.5-1.0 \times 10^9/L$, or if Platelets $= 50-100 \times 10^9/L$ **REDUCE** Gemcitabine to **75%** dose
3. On days 8 or 15, if $ANC < 1.0 \times 10^9/L$ OR if Platelets $< 50 \times 10^9/L$, **HOLD** dose for 1 week

Renal failure (Recommended action)

1. If $CrCl = 30-60 mL/min$ or Serum Creatinine $= 136-185 \mu mol/L$, reduce Cisplatin to **50%** dose
2. If $CrCl < 30 mL/min$ or Serum Creatinine $> 185 \mu mol/L$, **Omit** Cisplatin dose

Gastrointestinal Toxicities

1. If Mucositis or Diarrhea $\geq$ Grade 3 in previous course, **REDUCE** to **50%** dose

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

PATIENT VISIT

CHEMOTHERAPY PATIENT VISITS:
Approx. 2 hours

[Rev 07/02]

**CISPLATIN-IFOSFAMIDE-
ETOPOSIDE (VP-IP)**

Chemotherapy

(Testicular Cancer)

**ADVANCED LEVEL REGIMEN-
Provincial Cancer Centre**

PREHYDRATION

- Encourage patients to drink 6-8 glasses of water prior to chemo each day (increase fluids if poorly hydrated)

- May prehydrate with 1000mL Normal Saline; Infuse over 60 minutes

ETOPOSIDE 75mg/m² IV Days 1 to 5 (Round to nearest 10mg)

- Premixed in 1000mL bags of Normal Saline; Infuse over 60 minutes

- Give Etoposide BEFORE Cisplatin, to hydrate patient

CISPLATIN 20mg/m² IV Days 1 to 5 (Round to nearest 1mg)

- Mix drug in 500mL bag (Normal Saline); Infuse over 60 minutes

- May also admix 20G Mannitol (200mL of 10% solution) with Cisplatin

MESNA 240mg/m² IV 15 minutes before Ifosfamide dose

OR: **480mg/m² PO 15 minutes before Ifosfamide dose**

- Dilute in 100mL bag (Normal Saline); Infuse over 15 minutes

IFOSFAMIDE 1200mg/m² IV Days 1 to 5 (Round to nearest 100mg)

- Dilute in 500mL bag (Normal Saline); Infuse over 60 minutes

- May hydrate with 1-3L of IV fluid during infusion, to maintain high urine flow

MESNA 240mg/m² IV 4 & 8 hours after the start of each Ifosfamide dose

OR: **480mg/m² PO 4 & 8 hours after the start of each Ifosfamide dose**

- Dilute in 100mL bag (Normal Saline); Infuse over 15 minutes

POSTHYDRATION

- May prehydrate with 1000mL Normal Saline if additional hydration needed; Infuse over 60 minutes

- May add 10mEq/L KCl and 8 mmol/L MgSO₄ to Normal Saline

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

Days 1-5 - HIGH RISK Pre-Chemotherapy-

- Serotonin Receptor Antagonist prechemo each day (Ondansetron 8mg PO pre-chemo & 8mg PO qhs on Days 1 to 5, OR Granisetron 2mg PO prechemo each day, OR Dolasetron 100mg PO)- If patient has vomited on previous dose may give IV prechemo doses (Ondansetron 8mg IV; OR Granisetron 1mg IV, OR Dolasetron 100mg IV), **AND**
- Dexamethasone 8mg PO prechemo each day on Days 1 to 5- If patient has vomited on previous dose may give 8mg IV prechemo doses, or may increase Dexamethasone to 20mg PO/IV

Post-Chemotherapy-

- Dexamethasone 8mg PO q24h for 3 doses after last chemo treatment, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses after last chemo treatment, if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo

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GU-CIE

SUPPORTIVE CARE

HYPERSENSITIVITY REACTION:

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push
- *Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration (to prevent renal toxicity)*

CLINICAL MONITORING

- **Complete blood count** including differential, platelets and hemoglobin (CBC) and **serum electrolytes** (including Mg^{2+}) before each cycle of treatment
- Baseline and routine **renal function tests** [measured creatinine clearance, serum creatinine & BUN at baseline and before each cycle]
- **Clinical assessment of stomatitis**: oral examination upon patient complaint of a sore mouth
- Baseline and periodic **urine output** and **urinalysis tests (for RBCs)** before each cycle of treatment
- **Hepatic function tests** [serum Bilirubin levels] checked at baseline & before each cycle of treatment
- **Neurologic & Hearing** toxicity ratings (Cortical) at each visit

HEARING

- 0. No change
- 1. Asymptomatic
- 2. Tinnitus
- 0. Correctable hearing loss
- 1. Deafness

SENSORY

- 0. No change
- 1. Mild paraesthesia; no deep tendon reflex
- 2. Mild/moderate sensory loss; moderate paraesthesia
- 3. Sensory loss interferes with function

CYSTITIS

- 0. None
- 1. Mild symptoms
- 2. Symptoms relieved with therapy
- 3. Symptoms not relieved
- 4. Life-threatening

CORTICAL

- 0. None
- 1. Mild somnolence
- 2. Moderate somnolence
- 3. Severe somnolence, confusion, hallucination
- 4. Coma, seizures

Rated at each clinic visit

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

GU-CIE

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$ **OR** if Platelets $< 75 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Renal failure (Recommended actions)

1. If CrCl = 30-60mL/min or Serum Creatinine=136-185 μ mol/L, reduce Cisplatin to **50%** dose, and Etoposide to **75%** dose
2. If CrCl < 30 mL/min or Serum Creatinine $>185\mu$ mol/L, **Omit** Cisplatin dose and reduce Ifosfamide to **75%** dose
3. If CrCl < 12 mL/min, reduce Etoposide and Ifosfamide to **50%** dose

Urologic Toxicities

1. If RBC > 10 HPF, notify physician and **HOLD** Ifosfamide and continue Mesna

Hepatic dysfunction(Suggested actions)

1. If Bili=26-51 μ mol/L or AST=60-180IU/L, reduce Etoposide & Ifosfamide to **50%** dose
2. If Bili= 52-85 μ mol/L, reduce Etoposide & Ifosfamide to **25%** dose
3. If Bili $>85\mu$ mol/L or AST >180 IU/L, **Omit** Etoposide

PATIENT VISIT

CHEMOTHERAPY PATIENT VISITS:

Days 1 to 5: Approximately 3 hrs/day

GU

GU-CMV

**METHOTREXATE-
VINBLASTINE-CISPLATIN
(CMV) Chemotherapy**

(Bladder Carcinoma- Palliative Intent)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

METHOTREXATE 30mg/m²IV Days 1 & 8

- Push through sidearm of free flowing IV (Normal Saline)

VINBLASTINE 4mg/m²IV Days 1 & 8 (Round to nearest 0.1mg)

- Quick push through sidearm of free flowing IV (Normal Saline); Inject over 1 minute

PREHYDRATION IV Day 2

- Encourage patients to drink 6-8 glasses of water on Days 1, 2 & 3 (increase fluids if poorly hydrated)
- Normal Saline 1000mL; infuse over 1 hours
- Give 200mL of 10% Mannitol solution (20G); Infuse through sidearm concurrent with Cisplatin

CISPLATIN 100mg/m²IV Day 2 (Round to nearest 1mg)

- Mix drug in 500mL bag (Normal Saline); Infuse over 1 hour

POSTHYDRATION IV Day 2

- Normal Saline 1000mL; infuse over 1 hour
- May add 20mEq/L Potassium Chloride and 8mmol/L Magnesium Sulfate to Normal Saline
- Oral hydration by patient following chemotherapy (8-12 cups of fluid daily)

REPEAT EVERY 28 DAYS

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes (including Mg²⁺) before each cycle of treatment
- Baseline and routine renal function tests [measured creatinine clearance, serum creatinine & BUN at baseline and before each cycle]
- Hepatic function tests [serum Bilirubin levels] checked at baseline & before each cycle of treatment
- Baseline and periodic urine output and urinalysis tests
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth
- Neurologic toxicity ratings (Sensory) at each visit
- Baseline & periodic Hearing ratings; hearing tests if symptomatic

HEARING

0. No change
1. Asymptomatic
2. Tinnitus
3. Correctable hearing loss
4. Deafness

SENSORY

2. No change
3. Mild paraesthesia; no deep tendon reflex
4. Mild/moderate sensory loss; moderate paraesthesia
3. Sensory loss interferes with function

Rated at each clinic visit

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

Continued Next Page...

GU-CMV

SUPPORTIVE CARE

ANTIEMETIC REGIMENS:

Days 1 & 8- INTERMEDIATE RISK

Pre-Chemotherapy-

- Dopamine Receptor Antagonist PO Day 1 & Day 8 (Metoclopramide 10mg PO or Prochlorperazine 10mg PO)
- Dexamethasone 8mg PO Day 1 & Day 8

Day 2- HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), **AND**
- Dexamethasone 20mg IV **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
"When available in Canada"

Post-Chemotherapy- (after Day 2)

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *"When available in Canada"*

Post-Chemotherapy- (all other days)

- Dopamine Receptor Antagonist PO (Metoclopramide 10mg PO q4h PRN or Prochlorperazine 10mg PO q4h PRN)

DOSE MODIFICATION

Hematologic Toxicities:

1. If ANC < $1.5 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Hepatic dysfunction

1. If Bili=36-50 μ mol/L or AST =60-180IU/L, **reduce** Vinblastine to **50%** dose
2. If Bili= 51-85 μ mol/L or AST>180IU/L, **reduce** Vinblastine to **25%** & Methotrexate to **75%** dose
3. If Bili >85 μ mol/L, **Omit** Vinblastine & Methotrexate

Renal failure

1. If CrCl = 30-60mL/min or Serum Creatinine=136- 185 μ mol/L, **reduce** Cisplatin & Methotrexate to **50%** dose
2. If CrCl <30mL/min or Serum Creatinine>185 μ mol/L, **OMIT** Cisplatin & Methotrexate

PATIENT VISIT

CHEMOTHERAPY PATIENT VISITS:

Days 1 & 8 = Approx. 30 minutes
Day 2 = usually inpatient admission; if outpatient treatment 4 to 6 hours (depending on hydration)

[Rev 07/02]

GU-FU-CISP

5-FLUOROURACIL Infusion/ CISPLATIN

(Squamous Cell Carcinoma of the
Penis or Urethra)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

PREHYDRATION on Day 1

- Encourage patients to drink 6-8 glasses of water prior to chemo each day (increase fluids if poorly hydrated)
- May give Normal Saline 1000mL; Infuse over 1 hour
- May give 200mL of 10% Mannitol solution (20G); infuse through sidearm concurrent with Cisplatin

CISPLATIN 100mg/m² IV Day 1 (Round to nearest 1mg)

- Mix drug in 500mL Normal Saline; Infuse over 1 hour

POSTHYDRATION on Day 1

- Normal Saline 1000mL; infuse over 1 hour
- May add 10mEq/L KCl and 8 mmol/L MgSO₄ to Normal Saline

5-FLUOROURACIL 1000mg/m²/day CIV for 96 hours Starting on Day 1

- Continuous infusion using ambulatory infusion pump (Outpatient treatment)
- Admix in 1000mL Normal Saline and administer by Continuous Infusion over 96 hours; Infuse through patent peripheral venous catheter; Inspect peripheral infusion sites daily and replace if evidence of irritation or extravasation (Inpatient treatment) (Round to nearest 50mg)

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK- Day 1

Pre-Chemotherapy- Day 1

- Serotonin Receptor Antagonist IV (Ondansetron 8mg IV, OR Granisetron 1mg IV; OR Dolasetron 100mg IV), **AND**
- Dexamethasone 20mg IV PO **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy- (after Day 1 Cisplatin dose)

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *When available in Canada*

Post-Chemotherapy- (all other days)

- Dopamine Receptor Antagonist PO (Metoclopramide 10mg PO q4h PRN or Prochlorperazine 10mg PO q4h PRN)

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

Continued Next Page...

GU-FU-CISP

GU

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes (including Mg^{++}) before each cycle of treatment
- Baseline and routine **renal function tests** [measured creatinine clearance, serum creatinine & BUN at baseline and before each cycle]
- **Clinical assessment of stomatitis**, oral examination upon patient complaint of a sore mouth
- **Skin assessment**, especially extremities
- Baseline and routine **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels at baseline and before each cycle]

HEARING

- 0 No change
- 1 Asymptomatic
- 2 Tinnitus
- 3 Correctable hearing loss
- 4 Deafness

SENSORY

- 0 No change
- 1 Mild paraesthesia; no deep tendon reflex
- 2 Mild/moderate sensory loss, moderate paraesthesia
- 3 Sensory loss interferes with function
- 4 Deafness

Rated at each clinic visit

DOSE MODIFICATION

Hematologic Toxicities

1. If $ANC < 1.5 \times 10^9/L$, or if Platelets = $75-100 \times 10^9/L$, notify physician and **REDUCE** 5FU to 50% dose
2. If $ANC < 1.0 \times 10^9/L$ OR if Platelets $< 75 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Gastrointestinal Toxicities

1. If Mucositis or Diarrhea > Grade 3 in previous course, **REDUCE** to 50% dose of 5-FU

Renal failure

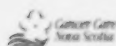
1. If Renal Function has not returned to normal ($CrCl > 60 mL/min$ or Serum Creatinine $< 136 \mu mol/L$) by Day 1 of cycle, **DISCONTINUE CISPLATIN** (Recommended action)

PATIENT VISIT

CHEMOTHERAPY PATIENT VISITS

Days 1 to 3 = 3 to 4 hours (depending upon hydration)

Day 5 = 15 minutes

**GU-GEMCIT****GEMCITABINE Chemotherapy**

(Bladder Carcinoma- Palliative Intent)

BASIC LEVEL REGIMEN-Community Hospital with
Oncology Nurses**GEMCITABINE 1000mg/m² IV Days 1, 8 and 15**(Dosing schedule may be adjusted for myelosuppression in each patient)
(Round to nearest 20mg)

- Mix drug in 250mL bag (Normal Saline); Infuse over 30 minutes through free-flowing IV

REPEAT EVERY 28 DAYS**SUPPORTIVE CARE****ANTIEMETIC REGIMEN:****INTERMEDIATE RISK**Pre-Chemotherapy-

- Dopamine Receptor Antagonist PO
(Prochlorperazine 10mg PO or
Metoclopramide 10mg PO)

Post-Chemotherapy-

- Dopamine Receptor Antagonist PO
(Prochlorperazine 10mg PO q4h
PRN OR Metoclopramide 10mg
POq4h PRN)

DOSE MODIFICATIONHematologic Toxicities

1. If ANC = $0.5 - 1.0 \times 10^9/L$, or if
Platelets = $50 - 100 \times 10^9/L$, notify
physician and **REDUCE**
Gemcitabine to **75%** dose
2. If ANC $< 1.0 \times 10^9/L$ OR if Platelets
 $< 50 \times 10^9/L$, notify physician and
HOLD dose for 1 week

Gastrointestinal Toxicities

1. If Mucositis or Diarrhea $\geq$ Grade 3
in previous course, **REDUCE** to
50% dose

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN****CLINICAL MONITORING**

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes (including Mg⁺⁺) before each cycle of treatment
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth
- Check for edema at each visit
- Routine toxicity ratings of Flu-like Symptoms, Lethargy at each visit

LETHARGY

0. None
1. Mild (Performance Status decreased by 1)
2. Moderate (Performance Status decreased by 2)
3. Severe (Performance Status decreased by 3)

FLU-LIKE SYMPTOMS

(Arthralgia, myalgia, diaphoresis, rigours/chills)

0. None
1. Mild
2. Moderate
3. Severe

Rated at each clinic visit**PATIENT VISIT****CHEMOTHERAPY PATIENT VISITS**

Approx. 45 minutes

GU-IFN-ALFA*SC

INTERFERON ALFA (Renal Cell Carcinoma) Therapy

(Metastatic Renal Cell Carcinoma - Palliative Intent)

Take-Home Prescription-
Special Authorization Required

INTERFERON ALFA 2-5MU/m² SC TIW

- May escalate up to 10MU/m² TIW (three times weekly), as tolerated (Outpatient prescription in multiples of 3, 5 or 10MU vials)

CONTINUOUS TREATMENT For a minimum of 2-3 months and until evidence of disease progression, if possible

SUPPORTIVE CARE

ANTIEMETIC REGIMEN NOT APPLICABLE

- Routine prophylaxis of flu-like symptoms with Acetaminophen 325-500mg tablets 1 or 2 tablets before each dose (especially if this adverse effect occurs with early doses)

NOTE

This regimen may only be used for good performance status patients with renal cell carcinoma, who can tolerate immunotherapy.

CLINICAL MONITORING

- Routine toxicity ratings of Flu-like Symptoms, Lethargy at follow-up visits

LETHARGY

0 None

1. Mild (Performance Status decreased by 1)

2. Moderate (Performance Status decreased by 2)

3. Severe (Performance Status decreased by 3)

FLU-LIKE SYMPTOMS

(*Arthralgia, myalgia, diaphoresis, rigours/chills*)

0 None

1 Mild

2. Moderate

3. Severe

Rated at monthly/quarterly clinic visit

GUIDELINE

See the CCNS website
www.cancercare.ns.ca for the
guideline on Interferon for Renal Cell
cancer

GU

GU-MVDC

METHOTREXATE-VINBLASTINE- DOXORUBICIN-CISPLATIN (M/VAC)

(Advanced Bladder Carcinoma-
Palliative Intent)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

PREHYDRATION Days 1 to 3

- Encourage patients to drink 6-8 glasses of water prior to chemo each day (increase fluids if poorly hydrated)
- May give Normal Saline 1000mL infuse over 1 hour
- May give 200mL of 10% Mannitol solution (20G); Infuse through sidearm concurrent with Cisplatin

METHOTREXATE 30mg/m² IV Days 1, 15 & 22 (Round to nearest 5mg)

- Slow push through sidearm of free flowing IV (Normal Saline)

VINBLASTINE 3mg/m² IV Days 2, 15 & 22 (Round to nearest 0.1mg)

- Direct IV push, (followed by a Normal Saline flush, if no IV line has been set up on Days 15 & 22)

DOXORUBICIN 30mg/m² IV Day 2 (Round to nearest 1mg)

- Reduce to 15mg/m² if prior radiotherapy to pelvis (>6000cGy)
- Slow push through sidearm of free flowing IV

CISPLATIN 70mg/m² IV Day 2 (Round to nearest 1mg)

- Mix drug in 500mL bag (Normal Saline); Infuse over 1 hour

POSTHYDRATION IV Day 2

- Normal Saline 1000mL; infuse over 1 hour
- May add 20mEq/L Potassium Chloride and 8mmol/L Magnesium Sulfate to Normal Saline
- Oral hydration by patient following chemotherapy (8-12 cups of fluid daily)

REPEAT EVERY 28 DAYS

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L OR if Platelets < 100 x 10⁹/L on Day 1, notify physician and **HOLD** dose for 1 week
2. If ANC = 1.0-1.5 x 10⁹/L, AND if Platelets ≥ 100 x 10⁹/L on Day 15 and or Day 22, notify physician and **REDUCE** Methotrexate and Vinblastine to **66%** dose levels
3. If ANC < 1.0 x 10⁹/L OR if Platelets < 100 x 10⁹/L on Day 15 and or Day 22, notify physician and **OMIT** doses of Methotrexate and Vinblastine

Hepatic dysfunction

1. If Bili=36-50µmol/L or AST =60-180IU/L, reduce Vinblastine & Doxorubicin to **50%** dose
2. If Bili= 51-85µmol/L or AST>180IU/L, reduce Vinblastine & Doxorubicin to **25%** dose & Methotrexate to **75%** dose
3. If Bili >85µmol/L, **Omit** Vinblastine, Doxorubicin & Methotrexate

Renal failure

1. If CrCl = 30-60mL/min or Serum Creatinine=136-185µmol/L, reduce Cisplatin & Methotrexate to **50%** dose
2. If CrCl <30mL/min or Serum Creatinine>185µmol/L, **OMIT** Cisplatin & Methotrexate
3. If Serum Creatinine>265µmol/L, **reduce** Doxorubicin to **25%** dose

Continued Next Page...

SUPPORTIVE CARE

ANTIEMETIC REGIMENS:

Days 1, 15 & 22- INTERMEDIATE RISK

Pre-Chemotherapy-

- Dopamine Receptor Antagonist PO (Metoclopramide 10mg PO, OR Prochlorperazine 10mg PO) **AND/OR**
- Dexamethasone 8mg PO Days 1, 15 & 22 & 8

Day 2- HIGH RISK

Pre-Chemotherapy- Day 2

- Serotonin Receptor Antagonist IV (Ondansetron 8mg IV, OR Granisetron 1mg IV, OR Dolasetron 100mg IV), **AND**
- Dexamethasone 20mg IV PO **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO) *"When available in Canada"*

Post-Chemotherapy- (after Day 2 Cisplatin dose)

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *"When available in Canada"*

Post-Chemotherapy- (all other days)

- Dopamine Receptor Antagonist PO (Metoclopramide 10mg PO q4h PRN, OR Prochlorperazine 10mg PO q4h PRN)

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

GU

GU-MVDC

CLINICAL MONITORING

- **Complete blood count** including differential, platelets and **hemoglobin (CBC)** and **serum electrolytes** (including Mg^{2+}) before each cycle of treatment
- Measured creatinine clearance before first cycle of chemotherapy
- Baseline and routine **renal function tests** [serum creatinine, serum electrolytes (including magnesium, calcium, potassium levels) & BUN] before Day 1 of each cycle of treatment
- **Liver function** [Bilirubin levels] checked at baseline and before each cycle of treatment
- Baseline **cardiac function tests** [MUGA scan] and periodic tests for all patients with cardiac risk factors or patients at or above the threshold dose levels
- Clinical exam for symptoms of **Congestive Heart Failure**
- Baseline and periodic **urine output** and **urinalysis tests** with high doses
- **Clinical assessment of stomatitis**: oral examination upon patient complaint of a sore mouth
- **Neurologic** toxicity ratings (Sensory) at each visit
- Baseline & periodic Hearing ratings; **hearing tests** if symptomatic

HEARING

- 0. No change
- 1. Asymptomatic
- 2. Tinnitus
- 3. Correctable hearing loss
- 4. Deafness

SENSORY

- 0. No change
- 1. Mild paraesthesia; no deep tendon reflex
- 2. Mild/moderate sensory loss; moderate paraesthesia
- 3. Sensory loss interferes with function

Rated at each clinic visit

PATIENT VISIT

CHEMOTHERAPY PATIENT VISITS

Days 1, 15 & 22 = Approx. 30 minutes
Day 2 = 4 to 6 hours (depending on hydration)

**VINBLASTINE-IFOSFAMIDE-
CISPLATIN (VIP)**

ADVANCED LEVEL REGIMEN-
Provincial Cancer Centre

Chemotherapy

(Salvage Regimen- Germ Cell/Testicular Cancer)

PREHYDRATION Days 1 to 5

- Encourage patients to drink 6-8 glasses of water prior to chemo each day (increase fluids if poorly hydrated)
- May give Normal Saline 1000mL; Infuse over 1 hour

VINBLASTINE 0.11mg/Kg IV Days 1 & 2 (Round to nearest 0.1mg)

- Quick push through sidearm of free flowing IV (Normal Saline); Inject over 1 minute

CISPLATIN 20mg/m² IV Days 1 to 5 (Round to nearest 1mg)

- Mix drug in 500mL bag (Normal Saline); Infuse over 60 minutes
- May also admix 20G Mannitol (200mL of 10% solution) with Cisplatin

MESNA 240mg/m² IV 15 minutes before Ifosfamide dose

- Dilute in 100mL bag (Normal Saline); Infuse over 15 minutes
- OR: **480mg/m²** PO 15 minutes before Ifosfamide dose

IFOSFAMIDE 1200mg/m² IV Days 1 to 5 (Round to nearest 100mg)

- Dilute in 500mL bag (Normal Saline); Infuse over 60 minutes
- May hydrate with 1-3L of IV fluid during infusion, to maintain high urine flow

MESNA 240mg/m² IV 4 & 8 hours after the start of each Ifosfamide dose

- Dilute in 100mL bag (Normal Saline); Infuse over 15 minutes
- OR: **480mg/m²** PO 4 & 8 hours after the start of each Ifosfamide dose

POSTHYDRATION Days 1 to 5

- May give 1000mL Normal Saline if additional hydration needed; Infuse over 60 minutes
- May add 10mEq/L potassium Chloride and 8 mmol/L Magnesium Sulphate to Normal Saline

REPEAT EVERY 21 DAYS

DOSE MODIFICATION

Urologic Toxicities

- 1 If RBC > 10 HPF, notify physician, **HOLD** Ifosfamide and continue Mesna

Hematologic Toxicities

- 1 If ANC < 1.5 x 10⁹/L OR if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Renal failure (Recommended actions)

- 1 If CrCl = 30-60mL/min or Serum Creatinine=136- 185µmol/L, reduce Cisplatin to **50%** dose, and Etoposide to **75%** dose
- 2 If CrCl <30mL/min or Serum Creatinine>185µmol/L, **Omit** Cisplatin dose and reduce Ifosfamide to **75%** dose
- 3 If CrCl < 12mL/min, reduce Ifosfamide to **50%** dose

Hepatic dysfunction(Suggested actions)

- 1 If Bili=36-50µmol/L or AST=60-180IU/L, **reduce** Vinblastine & Ifosfamide to **50%** dose
- 2 If Bili= 52-85µmol/L, **reduce** Vinblastine & Ifosfamide to **25%** dose
- 3 If Bili >85µmol/L or AST>180IU/L, **Omit** Etoposide

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SUPPORTIVE CARE

ANTIEMETIC REGIMEN: Days 1-5 - HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist prechemo each day (Ondansetron 8mg PO pre-chemo & 8mg PO qhs on Days 1 to 5; OR Granisetron 2mg PO prechemo each day; OR Dolasetron 100mg PO)- If patient has vomited on previous dose may give IV prechemo doses (Ondansetron 8mg IV; OR Granisetron 1mg IV; OR Dolasetron 100mg IV), **AND**
- Dexamethasone 8mg PO prechemo each day on Days 1 to 5- If patient has vomited on previous dose may give 8mg IV prechemo doses, or may increase Dexamethasone to 20mg PO/IV

Post-Chemotherapy-

- Dexamethasone 8mg PO q24h for 3 doses after last chemo treatment **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses after last chemo treatment, if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration (to prevent renal toxicity)

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes (including Mg²⁺) before each cycle of treatment
- Baseline and routine renal function tests [measured creatinine clearance, serum creatinine & BUN at baseline and before each cycle]
- Hepatic function tests [serum Bilirubin levels] checked at baseline & before each cycle of treatment
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth
- Baseline and periodic urine output and urinalysis tests (for RBCs)
- Neurologic & Hearing toxicity ratings (Cortical) at each visit

HEARING

- 0. No change
- 1. Asymptomatic
- 2. Tinnitus
- 0. Correctable hearing loss
- 1. Deafness

SENSORY

- 0. No change
- 1. Mild paraesthesia; no deep tendon reflex
- 2. Mild/moderate sensory loss; moderate paraesthesia
- 3. Sensory loss interferes with function

CYSTITIS

- 0. None
- 1. Mild symptoms
- 2. Symptoms relieved with therapy
- 3. Symptoms not relieved
- 4. Life-threatening

CORTICAL

- 0. None
- 1. Mild somnolence
- 2. Moderate somnolence
- 3. Severe somnolence, confusion, hallucination
- 4. Coma, seizures

Rated at each clinic visit

Continued Next Page...



GU-VIP

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

PATIENT VISIT
CHEMOTHERAPY PATIENT VISITS:
Days 1 to 5: Approximately 3 hrs/day

GU

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NOTE: *Regimen names in italics are not in this pocketbook version- See full version for drug monograph*

GY-CARBO

Carboplatin Chemotherapy (Recurrent Ovarian Cancer)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

PREHYDRATION

- Encourage patients to drink 6-8 glasses of water prior to chemo each day
- May prehydrate with 500mL Normal Saline; Infuse over 60 minutes

CARBOPLATIN AUC= 5 mg/mL/min (Range 5 to 7) IV day 1

- Mix in 250mL bag (5% Dextrose); Infuse over 60 minutes

POSTHYDRATION

- May give 500mL Normal Saline if additional hydration needed; Infuse over 30 minutes

REPEAT EVERY 21 DAYS For a Usual Total of 6 Cycles

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

INTERMEDIATE RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h on Days 1 to 3, OR Granisetron 1mg PO days 1 to 3, OR Dolasetron 100mg PO days 1 to 3), **AND**
- Dexamethasone 8 mg PO on Day 1
- Post-Chemotherapy-
- Dexamethasone 8 mg PO q24h for 3 doses starting Day 2, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
- No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
- Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes before each cycle of treatment
- Neurologic toxicity ratings (Sensory) at each visit
- Baseline and periodic renal function tests [serum creatinine, electrolytes & BUN]

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss, moderate paraesthesia
3. Sensory loss interferes with function

Rated at each clinic visit

GY

GY-CARBO

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$, notify physician and **HOLD** dose for 1 week (or until ANC $\geq 1.5 \times 10^9/L$)
2. If Platelets $< 100 \times 10^9/L$, **ADJUST** Carboplatin dose as described in Egorin formula

Renal failure (Recommended action)

1. If Serum Creatinine = 136-150 $\mu\text{mol/L}$ or Creatinine Clearance = 40-60 mL/min; **reduce** Carboplatin dose by **1mg/mL/min** (or by **50mg/m²** for BSA dosing)
2. If Serum Creatinine = 151-180 $\mu\text{mol/L}$ or Creatinine Clearance = 20-40 mL/min; **reduce** Carboplatin dose by **2mg/mL/min** (or by **100mg/m²** for BSA dosing)
3. If Serum Creatinine $> 181 \mu\text{mol/L}$ or Creatinine Clearance $< 20 \text{ mL/min}$, **DISCONTINUE** Carboplatin dose

NOTE

Calvert AUC Dosing Formula

DOSE (mg) = target AUC $\times$ (GFR + 25)

- GFR expressed as measured Creatinine clearance (mL/min) or estimated from serum Creatinine Creatinine Clearance (X60 for mL/min)

$$Cl_{Cr} \sigma^{\text{m}} = \frac{140 - \text{age (yrs)} \times \text{TBW (kg)}}{50 \times Cr_{\text{Serum}} (\mu\text{mol/L})}$$

(mL/sec)

$$Cl_{Cr} \text{ } \sigma^{\text{f}} (\text{mL/sec}) = Cl_{Cr} \sigma^{\text{m}} \times 0.85$$

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:

Approx. 1 1/2 hours

GY-BEP

CISPLATIN-ETOPOSIDE- BLEOMYCIN (PEB)

Chemotherapy

(Germ Cell Tumours)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

PREHYDRATION

- Encourage patients to drink 6-8 glasses of water prior to chemo each day (increase fluids if poorly hydrated)

- May prehydrate with 1000mL Normal Saline; Infuse over 60 minutes

ETOPOSIDE 100mg/m² IV daily Days 1 to 5 (Round to nearest 10mg)

- Premixed in 1000mL bags of Normal Saline; Infuse over 60 minutes

- Give Etoposide BEFORE Cisplatin, to hydrate patient

CISPLATIN 20mg/m² IV daily Days 1 to 5 (Round to nearest 1mg)

- Mix drug in 250mL bag (Normal Saline); Infuse over 60 minutes

- May also admix 20G Mannitol (200mL of 10% solution) with Cisplatin

BLEOMYCIN 30mg IV Days 2, 9 & 16

- Mix drug in 100mL bag (Normal Saline); Infuse over 15 minutes

- May give 1mg test dose before first treatment, observe for 30 minutes, then administer balance of dose if no reaction

- May give Diphenhydramine 25mg IV or Hydrocortisone 100mg IV before Bleomycin to prevent hypersensitivity reaction

POSTHYDRATION

- May give 1000mL Normal Saline if additional hydration needed; May add 10mEq/L KCl and 8mmol/L MgSO₄ to Normal Saline; Infuse over 60 minutes

REPEAT EVERY 21 DAYS For a Total of 3 to 4 Cycles

NOTE

Since this is first-line therapy for a cancer which may be cured for life, it is important to pay close attention to short-term treatment-related toxicities, to avoid possible long-term adverse effects. Aggressive hydration is recommended to prevent sub-clinical nephrotoxicity.

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L **OR** if Platelets < 100 x 10⁹/L on Day 1, notify physician and **HOLD** doses for 1 week

Renal failure (Recommended actions)

1. If CrCl < 30mL/min or SerCr > 185µmol/L, consider substituting Carboplatin for Cisplatin dose
2. If CrCl = 12-48mL/min, **REDUCE** Bleomycin to **75%** dose
3. If CrCl < 12mL/min, **REDUCE** Bleomycin to **50%** dose

GY-BEP

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: Days 1-5 - HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist prechemo each day (Ondansetron 8mg PO pre-chemo & 8mg PO qhs on Days 1 to 5; OR Granisetron 2mg PO prechemo each day; OR Dolasetron 100mg PO)- If patient has vomited on previous dose may give IV prechemo doses (Ondansetron 8mg IV; OR Granisetron 1mg IV; OR Dolasetron 100mg IV). **AND**
- Dexamethasone 8mg PO prechemo each day on Days 1 to 5- If patient has vomited on previous dose may give 8mg IV prechemo doses, or may increase Dexamethasone to 20mg PO/IV

Post-Chemotherapy-

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses after last chemo treatment, if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo. **AND**
- Dexamethasone 8mg PO q24h for 3 doses after last chemo treatment

Bleomycin ONLY days -LOW RISK

- After chemotherapy, may use a Dopamine Receptor Antagonist PRN (Metoclopramide 10mg PO q4h PRN or Prochlorperazine 10mg PO/PR q4h PRN)

HYPERSENSITIVITY PROPHYLAXIS:

- May give Diphenhydramine 25mg IV and/or Hydrocortisone 100mg IV before Bleomycin dose

HYPERSENSITIVITY REACTION:

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

GY-BEP

CLINICAL MONITORING

- **Complete blood count** including differential, platelets and hemoglobin (CBC) and serum electrolytes (including Mg^{2+}) before each cycle of treatment
- **Renal function tests** at baseline and before Day 1 of each cycle [measured creatinine clearance, serum creatinine, serum electrolytes (including magnesium, calcium, potassium levels) & BUN]
- **Liver function tests** at baseline and before Day 1 of each cycle [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]
- Tumour markers assessed at each cycle (AFP, β -hCG)
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Clinical pulmonary exam** at each visit, including pulmonary function tests, auscultation, pulmonary toxicity ratings (Cough, SOB)
- **Neurologic toxicity ratings** (Sensory) at each visit
- Baseline & periodic Hearing ratings; **hearing tests** if symptomatic

HEARING

- 0. No change
- 1. Asymptomatic
- 2. Tinnitus
- 1. Correctable hearing loss
- 2. Deafness

SENSORY

- 0. No change
- 1. Mild paraesthesia; no deep tendon reflex
- 2. Mild/moderate sensory loss; moderate paraesthesia
- 3. Sensory loss interferes with function

Rated at each clinic visit

COUGH

- 0. None
- 1. Mild
- 2. Moderate
- 3. Severe

SHORT OF BREATH

- 0. No change
- 1. Mild SOB
- 2. Dyspnea on exertion
- 3. Dyspnea at normal level of activity
- 4. Dyspnea at rest

Rated at each clinic visit, if Bleomycin dosage needs adjustment

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

PATIENT VISIT

CHEMOTHERAPY PATIENT VISITS:
Days 1 to 5: Approx. 3 hrs/day
Bleomycin Days: Approx. 30 min

GY

GY-CISP

Cisplatin (Cervix)

Chemotherapy

(Cervical Cancer-Palliative)

INTERMEDIATE LEVEL REGIMEN-

Regional Hospital with Dedicated
Cancer Treatment Unit

PREHYDRATION

- Encourage patients to drink 6-8 glasses of water prior to chemo each day (increase fluids if poorly hydrated)
- Normal Saline 1000mL infuse over 1 hours before chemotherapy

CISPLATIN 75mg/m² IV Day 1 (Round to nearest 1mg)

- Mix drug in 500mL bag (Normal Saline); Infuse over 60 minutes
- May also give 250mL of 20%Mannitol solution (50G); infuse through sidearm concurrent with Cisplatin (if diuresis needed)

POSTHYDRATION

- Normal Saline 1000mL infuse over 1 hour (increase fluids if poor oral intake)
- May add 10mEq/L KCl and 8 mmol/L MgSO₄ to Normal Saline
- Oral hydration by patient following chemotherapy (8-12 cups of fluid daily)

REPEAT EVERY 21 DAYS For a Usual Total of 6 Cycles

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy:

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV). **AND**
- Dexamethasone 20mg IV **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
"When available in Canada"

Post-Chemotherapy:

- Dexamethasone 8 mg PO q24h for 3 doses. **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) "When available in Canada"
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration

PHYSICIAN'S STANDING ORDERS

AVAILABLE FOR THIS REGIMEN

GY-CISP

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Baseline and routine renal function tests [serum creatinine, electrolytes (including Mg^{++}) & BUN]- before each treatment cycle
- Neurologic toxicity ratings (Sensory) at each visit
- Baseline & periodic Hearing ratings, hearing tests if symptomatic

HEARING

0. No change
1. Asymptomatic
2. Tinnitus
3. Correctable hearing loss
4. Deafness

SENSORY

0. No change
1. Mild paraesthesia, no deep tendon reflex
2. Mild/moderate sensory loss, moderate paraesthesia
3. Sensory loss interferes with function

Rated at each clinic visit

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$ OR if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Renal failure

1. If CrCl = 30-60mL/min or Serum Creatinine=136-185 μ mol/L; reduce to **50%** dose
2. If CrCl < 30 mL/min or Serum Creatinine $>185\mu$ mol/L; **Omit** dose (Recommended action)

Hepatic dysfunction

1. If Bili=26-51 μ mol/L or AST=60-180IU/L, reduce to **50%** dose
2. If Bili= 52-85 μ mol/L, reduce to **25%** dose
3. If Bili $>85\mu$ mol/L or AST >180 IU/L, **Omit** dose (Suggested action)

PATIENT VISIT

CHEMOTHERAPY VISIT:

- 4 to 6 hours (depending on hydration)

GY

GY-CISP*W

Cisplatin Concurrent (Cervix)

Chemoradiotherapy

(Cervical Cancer) -Concurrent

Radiotherapy

ADVANCED LEVEL REGIMEN-

Provincial Cancer Centre

PREHYDRATION

- Encourage patient to drink 6-8 glasses of water prior to chemo each day
- Prehydrate with 500mL Normal Saline; Infuse over 1 hour

CISPLATIN 40mg/m² IV Days 1, 8, 15, 22 & 29 (Round to nearest 1mg)

- Mix drug in 500mL bag (Normal Saline); Infuse over 60 minutes;
- May also give 250mL of 20% Mannitol solution (50G); infuse through sidearm concurrent with Cisplatin (if diuresis needed)

POSTHYDRATION

- 500mL Normal Saline (may add 10mEq/500mL PotassiumChloride & 8mmol/500mL Magnesium Sulfate); Infuse over 1 hour (increase fluids if poor oral intake)

REPEAT EVERY 7 DAYS DURING RADIOTHERAPY

For a Usual Total of 5 Cycles

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), **AND**
- Dexamethasone 20mg IV **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO) *"When available in Canada"*

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *"When available in Canada"*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration

PHYSICIAN'S STANDING ORDERS

AVAILABLE FOR THIS REGIMEN

GY-CISP*W

CLINICAL MONITORING

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Baseline and routine renal function tests** [serum creatinine, electrolytes (including Mg^{2+}) & BUN]- before each treatment cycle
- **Neurologic toxicity ratings** (Sensory) at each visit
- **Baseline & periodic Hearing ratings; hearing tests** if symptomatic

HEARING

0. No change
1. Asymptomatic
2. Tinnitus
3. Correctable hearing loss
4. Deafness

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss; moderate paraesthesia
3. Sensory loss interferes with function

Rated at each clinic visit

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < $1.5 \times 10^9/L$ OR if Platelets < $100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Renal failure

1. If CrCl = 30-60mL/min or Serum Creatinine=136-185 μ mol/L; reduce to **50%** dose
2. If CrCl < 30mL/min or Serum Creatinine>185 μ mol/L; **Omit** dose (*Recommended action*)

Hepatic dysfunction

1. If Bili=26-51 μ mol/L or AST=60-180IU/L, reduce to **50%** dose
2. If Bili= 52-85 μ mol/L, reduce to **25%** dose
3. If Bili >85 μ mol/L or AST>180IU/L, **Omit** dose (*Suggested action*)

PATIENT VISIT

CHEMOTHERAPY VISIT:

4 to 6 hours (depending on hydration)

GY

GY-DACTIN

Dactinomycin Chemotherapy

(Gestational Trophoblast Disease -
Low Risk)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

DACTINOMYCIN 1.25mg/m² IV Day 1

- Slow push through sidearm of free flowing IV

REPEAT EVERY 14 DAYS For a Usual Total of 1 Cycle After
Normal HCG Titre

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy:

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV) **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO) *"When available in Canada"*

Post-Chemotherapy:

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
- No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
- Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *"When available in Canada"*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)

CLINICAL MONITORING

- Beta HCG titres each week during treatment
- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Liver function tests at baseline and before each cycle of chemotherapy [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]
- Baseline renal function tests (if failure suspected) [serum creatinine, electrolytes & BUN]
- Clinical assessment of stomatitis: oral examination upon patient complaint of a sore mouth
- Local Site Toxicity ratings, if incident of phlebitis

Local Site Toxicity

0. None
 1. Pain
 2. Pain & inflammation; phlebitis
 3. Ulceration
 4. Plastic surgery
- Upon Patient Complaint Or
Clinical Event**

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

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GY-DACTIN

DOSE MODIFICATION

HCG Titre

1. If HCG Titre rises (10 fold or more), notify physician and **HOLD** dose for 1 week; if HCG Titre continues to rise, **Discontinue** Dactinomycin
2. If HCG Titre plateaus for 2 or more weeks, notify physician and **Discontinue** Dactinomycin

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Hepatic failure:

1. Consider dose reduction if LFTs elevated (e.g. Bilirubin or AST)

PATIENT VISIT

CHEMOTHERAPY VISIT:

Approximately 30 to 45 minutes

GY

GY-DOXO-CISP

Doxorubicin-Cisplatin

Chemotherapy

(Endometrial Cancer)

INTERMEDIATE LEVEL REGIMEN

Regional Hospital with Dedicated
Cancer Treatment Unit

PREHYDRATION

- Encourage patient to drink 6-8 glasses of water prior to chemo each day
- Prehydrate with 500mL Normal Saline; Infuse over 1 hour

DOXORUBICIN 65mg/m² IV Day 1 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV

CISPLATIN 65mg/m² IV Day 1 (Round to nearest 1mg)

- Mix drug in 500mL bag (Normal Saline); Infuse over 60 minutes;
- May also give 300mL of 10% Mannitol solution (30G); infuse through sidearm concurrent with Cisplatin (if diuresis needed)

POSTHYDRATION

- May give 500mL Normal Saline (may add 10mEq/500mL Potassium Chloride & 8mmol/500mL Magnesium Sulphate); Infuse over 1 hour (increase fluids if poor oral intake)

REPEAT EVERY 21 DAYS For a Usual Total of 6 Cycles

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), **AND**
- Dexamethasone 20mg IV **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *When available in Canada*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration

PHYSICIAN'S STANDING ORDERS

AVAILABLE FOR THIS REGIMEN

Continued Next Page...

GY-DOXO-CISP

CLINICAL MONITORING

- **Complete blood count including differential, platelets and hemoglobin (CBC) and electrolytes** [including Mg^{2+}] before each cycle of treatment
- **Serum creatinine** at baseline and before Day 1 each cycle
- **Liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels] at baseline and before Day 1 each cycle
- Clinical exam for symptoms of **Congestive Heart Failure**
- Periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels
- **Neurologic toxicity ratings** (Sensory) at each visit
- Baseline & periodic Hearing ratings; **hearing tests** if symptomatic

HEARING

0. No change
1. Asymptomatic
2. Tinnitus
3. Correctable hearing loss
4. Deafness

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss; moderate paraesthesia
3. Sensory loss interferes with function

Rated at each clinic visit

DOSE MODIFICATION

Hematologic Toxicities

1. If $ANC < 1.5 \times 10^9/L$ OR if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Renal failure (Recommended action)

1. If Creatinine Clearance = 30-60mL/min or Serum Creatinine=136-185 μ mol/L; **reduce** Cisplatin to **50%** dose
2. If Creatinine Clearance < 30 mL/min or Serum Creatinine $>185\mu$ mol/L; **Omit** Cisplatin dose

Hepatic dysfunction (Suggested action)

1. If Bili=26-51 μ mol/L or AST=60-180IU/L, **reduce** Cisplatin to **50%** dose and Doxorubicin to **50%** dose
2. If Bili= 52-85 μ mol/L, **reduce** Cisplatin to **25%** dose and Doxorubicin to **25%** dose
3. If Bili $>85\mu$ mol/L or AST >180 IU/L, **Omit** all drugs

PATIENT VISIT

CHEMOTHERAPY VISIT:

4 to 6 hours (depending on hydration)

GY

GY-EPI-CISP

Epirubicin-Cisplatin

Chemotherapy

(Endometrial Cancer)

INTERMEDIATE LEVEL REGIMEN-

Regional Hospital with Dedicated

Cancer Treatment Unit

PREHYDRATION

- Encourage patient to drink 6-8 glasses of water prior to chemo each day
- Prehydrate with 500mL Normal Saline; Infuse over 1 hour

EPIRUBICIN 65mg/m² IV Day 1 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV

CISPLATIN 65mg/m² IV Day 1 (Round to nearest 1mg)

- Mix drug in 500mL bag (Normal Saline); Infuse over 60 minutes;
- May also give 300mL of 10% Mannitol solution (30G); infuse through sidearm concurrent with Cisplatin (if diuresis needed)

POSTHYDRATION

- May give 500mL Normal Saline (may add 10mEq/500mL Potassium Chloride & 8mmol/500mL Magnesium Sulphate); Infuse over 1 hour (increase fluids if poor oral intake)

REPEAT EVERY 21 DAYS For a Usual Total of 6 Cycles

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), **AND**
- Dexamethasone 20mg IV **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *When available in Canada*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration

PHYSICIAN'S STANDING ORDERS

AVAILABLE FOR THIS REGIMEN

Continued Next Page...

GY-EPI-CISP

CLINICAL MONITORING

- **Complete blood count** including differential, platelets and hemoglobin (CBC) and **electrolytes** [including Mg^{2+}] before each cycle of treatment
- **Serum creatinine** at baseline and before Day 1 each cycle
- **Liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels] at baseline and before Day 1 each cycle
- Clinical exam for symptoms of **Congestive Heart Failure**
- Periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels
- **Neurologic toxicity ratings** (Sensory) at each visit
- Baseline & periodic Hearing ratings: **hearing tests** if symptomatic

HEARING

0. No change
1. Asymptomatic
2. Tinnitus
3. Correctable hearing loss
4. Deafness

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss; moderate paraesthesia
3. Sensory loss interferes with function

Rated at each clinic visit

DOSE MODIFICATION

Hematologic Toxicities

1. If $ANC < 1.5 \times 10^9/L$ OR i If Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Renal failure (*Recommended action*)

1. If Creatinine Clearance = 30-60mL/min or Serum Creatinine=136-185 μ mol/L; **reduce** Cisplatin to **50%** dose
2. If Creatinine Clearance < 30 mL/min or Serum Creatinine > 185 μ mol/L; **Omit** Cisplatin dose

Hepatic dysfunction (*Suggested action*)

1. If Bili=26-51 μ mol/L or AST=60-180IU/L, **reduce** Cisplatin to **50%** dose and Epirubicin to **50%** dose
2. If Bili= 52-85 μ mol/L, **reduce** Cisplatin to **25%** dose and Epirubicin to **25%** dose
3. If Bili > 85 μ mol/L or AST > 180 IU/L, **Omit** all drugs

PATIENT VISIT

CHEMOTHERAPY VISIT:

4 to 6 hours (depending on hydration)

GY

GY-EMA-CO

**Etoposide-Methotrexate-
Dactinomycin/
Cyclophosphamide-Vincristine
(EMA-CO)**

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

(Gestational Trophoblast Disease - High Risk/Metastatic)

ETOPOSIDE 100mg/m² IV Days 1 & 2

- Premixed in 500mL bag of Normal Saline; connect piggyback to IV line; Infuse over 60 minutes; (For doses >200mg, mix in 600mL and infuse over 90 minutes)
- Adjust rate if blood pressure drops

DACTINOMYCIN 0.5mg IV Days 1 & 2

- Slow push through sidearm of free flowing IV (Normal Saline) over 1-5 minutes

METHOTREXATE 100mg/m² IV Day 1

- Mix in 100mL bag (Normal Saline); Infuse over 30 minutes
Followed by:

METHOTREXATE 200mg/m² CIV (over 12 hours) Day 1

- Mix in 500mL bag (Normal Saline); Infuse over 12 hours

**LEUCOVORIN 15mg PO q6h for 4 doses, starting 24 hours after starting
Methotrexate**

VINCRIStINE 1mg/m² IV Day 8

- Quick push through sidearm of free flowing IV (Normal Saline); Inject over at least 1 minute

CYCLOPHOSPHAMIDE 600mg/m² IV Day 8

- Mix in 250mL bag (Normal Saline); Infuse over 60 minutes

REPEAT EVERY 21 DAYS For a Usual Total of 2 to 4 Cycles After
Normal HCG Titre

SUPPORTIVE CARE

ANTIEMETIC REGIMENS: Day 1 - HIGH RISK

Pre-Chemotherapy on Days 1 & 2-

- Serotonin Receptor Antagonist IV (Ondansetron 8mg IV prechemo and 8mg IV qhs; **OR** Granisetron 1mg IV prechemo; **OR** Dolasetron 100mg IV prechemo), **AND**

- Dexamethasone 8mg IV prechemo (may increase to 20mg IV)

Post-Chemotherapy-

- Dexamethasone 8 mg PO/IV q24h for 3 doses, **AND**

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**

- No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**

- Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

Continued Next Page...

SUPPORTIVE CARE

Day 8 - INTERMEDIATE RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO; **OR** Granisetron 2mg PO; **OR** Dolasetron 100mg PO), **AND**
- Dexamethasone 8mg PO (may increase to 20mg IV)

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses; **OR** Granisetron 2mg PO q24h for 1 dose; **OR** Dolasetron 100mg PO q24h for 1 dose)

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

CLINICAL MONITORING

- **Beta HCG titres** each week during treatment
- **Complete blood count including differential, platelets and hemoglobin (CBC) and electrolytes** on Days 1 & 8 each cycle of treatment
- **Serum creatinine** at baseline and before Day 1 of each cycle
- **Liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels] at baseline and before each cycle of treatment
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- Baseline **blood pressure** at each treatment (Days 1 & 2); monitor for hypotension
- **Urinalysis (RBCs)**- periodic and in response to patient complaint
- **Neurologic** toxicity ratings (Sensory, Constipation) at each visit

CONSTIPATION

0. No change
1. Mild
2. Moderate
3. Severe
4. Ileus >96 hours

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss; moderate paraesthesia
3. Sensory loss interferes with function

Rated at each clinic visit

PATIENT VISIT

CHEMOTHERAPY VISITS: Days 1 & 2

Given in hospital

Day 8 = Approximately 1½ hours

GY-LIPO-DOXO

Pegylated Liposomal Doxorubicin Chemotherapy (Ovarian Cancer- Palliative Treatment)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

PREMEDICATIONS:

DEXAMETHASONE 20mg PO 12 & 6 hours before Liposomal Doxorubicin
DIPHENHYDRAMINE 50mg IV & RANITIDINE 50mg IV

- Admixed together in 50mL minibag of Normal Saline; Give over 15 minutes, starting 30 minutes before Liposomal Doxorubicin

Liposomal DOXORUBICIN (Pegylated) 40mg/m² IV Day 1

- Mix in 250mL bag (5% Dextrose ONLY); do NOT use an in-line filter
- Infuse first dose at 1mg/minute; infuse all subsequent doses over 1 hour

REPEAT EVERY 28 DAYS

GY

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK Pre Chemotherapy-

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO; **OR** Granisetron 2mg PO; **OR** Dolasetron 100mg PO), **AND**
- Dexamethasone 8mg PO (may increase to 20mg IV)

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 days, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses; **OR** Granisetron 2mg PO q24h for 1 dose; **OR** Dolasetron 100mg PO q24h for 1 dose)

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Liver function tests [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels] before each cycle of treatment
- Observation for hypersensitivity reaction, pulse rate and blood pressure during and for 30 minutes after injection (emergency treatment readily available)
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth
- Clinical assessment of hands and feet; rate grade of hand-foot skin reaction (palmar-plantar-erythrodysesthesia)

HAND-FOOT SKIN REACTION

0. none
1. skin changes or dermatitis without pain (e.g. erythema, peeling)
2. skin changes with pain, not interfering with function
3. skin changes with pain, interfering with function

Continued Next Page...

GY-LIPO-DOXO

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, notify physician and

HOLD dose for 1 week

Hepatic dysfunction:

1. If serum bilirubin = $21-51 \mu\text{mol/L}$, reduce to **50%**
2. If serum bilirubin $> 51 \mu\text{mol/L}$, give **25%** of normal dose.

Palmar-plantar-erythrodysesthesia:

1. If grade 2/3/4 after week 4 of treatment, **HOLD** dose for 1 week;
2. After week 5 of treatment:
 - If grade 1: reduce to **25%** dose
 - If grade 2: reduce to **50%** dose
 - If grade 3: discontinue the treatment

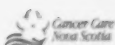
Stomatitis:

1. If grade 2: **HOLD** dose for 1 week
2. If grade 3: **HOLD** dose for 1 week, then reduce to **25%** dose
3. If grade 4: **HOLD** dose for 1 week, then reduce to **50%** dose.

PATIENT VISIT

CHEMOTHERAPY VISIT:

Approximately 90 to 120 minutes

**GY-ETOP*PO****Oral Etoposide
Chemotherapy***(Advanced Ovarian Cancer)***Take-Home Prescription-
Unrestricted****ETOPOSIDE 50 - 100mg PO daily for 14 - 21 days****REPEAT EVERY 28 DAYS****SUPPORTIVE CARE****ANTIEMETIC REGIMEN: LOW RISK**

- Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10mg PO q3-4h PRN

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth

DOSE MODIFICATION

If ANC $< 1.5 \times 10^9/L$, notify physician and **HOLD** dose (Until ANC $\geq 1.5 \times 10^9/L$)

GY

[Rev 11/01]

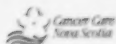
**GY-MEDROXYP****Medroxyprogesterone
Chemotherapy***(Endometrial Cancer)***Take-Home Prescription-
Unrestricted****MEDROXYPROGESTERONE 100mg PO BID to QID***(Outpatient prescription in multiples of 100mg tablets)***SUPPORTIVE CARE**

**ANTIEMETIC REGIMEN: NOT
APPLICABLE**

CLINICAL MONITORING

- Baseline pregnancy test

[Rev 11/01]

**GY-MEGES****Megestrol Therapy**

(Endometrial Cancer)

**Take-Home Prescription-
Unrestricted****MEGESTROL 160mg** PO daily

(Outpatient prescription in multiples of 40mg & 160mg tablets)

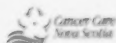
CONTINUOUS TREATMENT**SUPPORTIVE CARE**ANTIEMETIC REGIMEN NOT
APPLICABLE**CLINICAL MONITORING**

- Baseline pregnancy test

NOTE

- Prescription costs covered by all third party prescription plans
- To reduce drug costs, it is advisable to prescribe in lots of 3 months (or longer) once treatment is established. This will reduce cost to the patient or prescription plan.

[Rev 11/01]

**GY-MELPH *OV****Oral Melphalan
Chemotherapy**

(Ovarian Cancer)

**Take-Home Prescription-
Unrestricted****MELPHALAN 0.25mg/Kg** PO daily for 4 days

(Outpatient prescription in multiples of 2mg tablets)

REPEAT EVERY 28 DAYS**SUPPORTIVE CARE**ANTIEMETIC REGIMEN NOT
APPLICABLE**CLINICAL MONITORING**

- Complete blood count including differential, platelets and hemoglobin (CBC), and serum electrolytes before each cycle of treatment

DOSE MODIFICATION

If ANC $< 1.5 \times 10^9/L$, notify physician and **HOLD** dose for 1 week OR If Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

[Rev 11/01]

GY-METHO

Methotrexate Chemotherapy

(Gestational Trophoblast Disease -
Low Risk)

BASIC LEVEL REGIMEN-

Community Hospital with
Oncology Nurses

METHOTREXATE 30mg/m² IM Day 1

(Round to nearest 5mg- To a maximum dose of 60mg)

REPEAT EVERY 7 DAYS For a Usual Total of 1 Cycle After
Normal HCG Titre

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

Pre Chemotherapy-

- No routine antiemetic before chemotherapy

OR

- If vomiting in prior cycle, may give a Dopamine Receptor Antagonist PO prechemo (Metoclopramide 10mg PO; **OR** Prochlorperazine 10mg PO)

Post Chemotherapy-

- May give a Dopamine Receptor Antagonist PO (Prochlorperazine 10mg PO q4-6h PRN; **OR** Metoclopramide 10mg PO q4-6h PRN)

CLINICAL MONITORING

- **Beta HCG titres** each week during treatment
- **Complete blood count** including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- **Baseline renal function tests** [serum creatinine, electrolytes & BUN] and **serum creatinine** before Day 1 each treatment (i.e. each week)
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels] before each cycle of treatment

DOSE MODIFICATION

HCG Titre

1. If HCG Titre rises (10 fold or more), notify physician and **HOLD** dose for 1 week; if HCG Titre continues to rise, **Discontinue** Methotrexate
2. If HCG Titre plateaus for 2 or more weeks, notify physician and **Discontinue** Methotrexate

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Renal failure (Suggested action)

1. If CrCl = 12-48mL/min or Serum Creatinine = 100- 180µmol/L, **reduce** Methotrexate to **50%** dose
2. If CrCl < 12mL/min or Serum Creatinine > 180µmol/L, **Omit** Methotrexate dose

Hepatic dysfunction

1. If Bili = 50-85µmol/L or AST > 180IU/L, **reduce** Methotrexate to **75%** dose
2. If Bili > 85µmol/L, **Omit** Methotrexate dose

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

PATIENT VISIT

CHEMOTHERAPY VISIT:
Approximately 30 to 45 minutes

[Rev 09/02]

GY-PACLI

Paclitaxel Chemotherapy

(Advanced Ovarian Cancer)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

PREMEDICATIONS:

DEXAMETHASONE 20mg PO 12 & 6 hours before Paclitaxel

OR- 20mg IV starting 45 minutes before Paclitaxel

DIPHENHYDRAMINE 50mg IV & RANITIDINE 50mg IV

- Admixed together in 50mL minibag of Normal Saline; Give over 15 minutes, starting 30 minutes before Paclitaxel

PACLITAXEL 175mg/m² IV Infuse over 3 hours Day 1 (Round to nearest 3mg)

- Mix in 500mL bag (5% Dextrose- dilution concentration 0.3-1.2 mg/mL); Use non-PVC equipment, including 0.22 micron in-line filter; Infuse over 3 hours
- Take a baseline blood pressure measurement, if prior hypotension

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: INTERMEDIATE RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO; OR Granisetron 2mg PO; OR Dolasetron 100mg PO)

OR

- Dopamine Receptor Antagonist PO (Metoclopramide 10mg PO, or Prochlorperazine 10mg PO)

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- May give a Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO/ 10mg PR q4h PRN post chemo **OR** Metoclopramide 10mg PO q4-6h PRN post chemo)

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

GY

GY-PACLI

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Liver function tests [GGT, ALT, AST & Bilirubin levels] before each cycle of treatment
- Watch for symptoms of **fever or infection**
- **Neurologic** (Sensory) , hypersensitivity and flu-like symptoms toxicity ratings at each visit
- Baseline **blood pressure** and **pulse rate monitoring** during drug administration & for the following hour

SENSORY

- 0 No change
- 1 Mild paraesthesia, no deep tendon reflex
- 2 Mild/moderate sensory loss; moderate paraesthesia
- 3 Sensory loss interferes with function

FLU-LIKE SYMPTOMS

(Arthralgia, myalgia)

- 0 None
- 1 Mild
- 2 Moderate
- 3 Severe

HYPERSENSITIVITY/ALLERGY

- 0 None
- 1 Transient rash, fever $<38^{\circ}\text{C}$
- 2 Urticaria, fever $\geq 38^{\circ}\text{C}$, mild bronchospasm
- 3 Serum sickness, bronchospasm, requires parenteral meds
- 4 Anaphylaxis

Rated at each clinic visit

DOSE MODIFICATION

Hematologic Toxicities

1. If $\text{ANC} < 1.5 \times 10^9/\text{L}$, or if Platelets $< 100 \times 10^9/\text{L}$, notify physician and **HOLD** dose for 1 week

Hepatic dysfunction (Suggested action)

1. If $\text{AST} > 70\text{IU/L}$ or $\text{Bili} < 25\mu\text{mol/L}$, give **Maximum dose of 135mg/m²**
2. If $\text{Bili} = 25\text{--}50\mu\text{mol/L}$, give **Maximum dose of 75mg/m²**
3. If $\text{Bili} > 50\mu\text{mol/L}$, give **Maximum dose of 50mg/m²**

GUIDELINE

See the CCNS website www.cancercare.ns.ca for the guideline on Paclitaxel for ovarian cancer

PATIENT VISIT

CHEMOTHERAPY VISIT:
Approximately 5 hours

**GY-PACLI-CARBO****Paclitaxel-Carboplatin
Chemotherapy**

(Ovarian Cancer)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit**PREMEDICATIONS:**

DEXAMETHASONE 20mg PO 12 & 6 hours before Paclitaxel

OR- 20mg IV starting 45 minutes before Paclitaxel

DIPHENHYDRAMINE 50mg IV & RANITIDINE 50mg IV

- Admixed together in 50mL minibag of Normal Saline; Give over 15 minutes, starting 30 minutes before Paclitaxel

PACLITAXEL 175mg/m² IV Infuse over 3 hours Day 1

(Round to nearest 3mg)

- Mix in 500mL bag (5% Dextrose- dilution concentration 0.3-1.2 mg/mL); Use non-PVC equipment, including 0.22 micron in-line filter; Infuse over 3 hours
- Take a baseline blood pressure measurement, if prior hypotension

CARBOPLATIN AUC= 5 mg/mL/min IV Day 1

- Mix in 250mL bag (5% Dextrose); Infuse over 30 (Round to nearest 5mg)
- May infuse concurrently with Paclitaxel, using a Y-connector

REPEAT EVERY 21 DAYS**SUPPORTIVE CARE****ANTIEMETIC REGIMEN: INTERMEDIATE RISK**Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO; OR Granisetron 2mg PO; OR Dolasetron 100mg PO)

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- May give a Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO/ 10mg PR q4h PRN post chemo **OR** Metoclopramide 10mg PO q4-6h PRN post chemo)

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

Continued Next Page...

GY-PACLI-CARBO

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes (including Mg^{2+}) before each cycle of treatment
- Serum creatinine level at baseline and before each cycle of chemotherapy
- Liver function tests [GGT, ALT, AST & Bilirubin levels] before each cycle of treatment
- Watch for symptoms of fever or infection
- Neurologic (Sensory), hypersensitivity and flu-like symptoms toxicity ratings at each visit
- Baseline blood pressure and pulse rate monitoring during drug administration & for the following hour

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss; moderate paraesthesia
3. Sensory loss interferes with function

FLU-LIKE SYMPTOMS

(Arthralgia, myalgia)

0. None
1. Mild
2. Moderate
3. Severe

HYPERSENSITIVITY/ALLERGY

0. None
1. Transient rash, fever $<38^{\circ}\text{C}$
2. Urticaria, fever $\geq 38^{\circ}\text{C}$, mild bronchospasm
3. Serum sickness, bronchospasm, requires parenteral meds
4. Anaphylaxis

Rated at each clinic visit

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/\text{L}$, or if Platelets $< 100 \times 10^9/\text{L}$, notify physician and **HOLD** dose for 1 week

Hepatic dysfunction (Suggested action)

1. If Bili $\geq 25\mu\text{mol/L}$, give Paclitaxel maximum dose of $135\text{mg}/\text{m}^2$
2. If Bili = $26\text{--}51\mu\text{mol/L}$ or AST = $60\text{--}180\text{IU/L}$, give Paclitaxel maximum dose of $75\text{mg}/\text{m}^2$
3. If Bili = $52\text{--}85\mu\text{mol/L}$, give Paclitaxel maximum dose of $50\text{mg}/\text{m}^2$

Renal failure (Recommended action)

1. If Serum Creatinine = $136\text{--}150\mu\text{mol/L}$ or Creatinine Clearance = $40\text{--}60\text{mL}/\text{min}$, **reduce** Carboplatin dose by $1\text{mg}/\text{mL}/\text{min}$ (or by $50\text{mg}/\text{m}^2$ for BSA dosing)
2. If Serum Creatinine = $151\text{--}180\mu\text{mol/L}$ or Creatinine Clearance = $20\text{--}40\text{mL}/\text{min}$, **reduce** Carboplatin dose by $2\text{mg}/\text{mL}/\text{min}$ (or by $100\text{mg}/\text{m}^2$ for BSA dosing)
3. If Serum Creatinine $> 181\mu\text{mol/L}$ or Creatinine Clearance $< 20\text{mL}/\text{min}$, **OMIT** Carboplatin dose

GY-PACLI-CARBO

NOTE

Calvert AUC Dosing Formula

DOSE (mg)=target AUC x (GFR + 25)

• GFR expressed as measured

Creatinine clearance (mL/min) or

estimated from serum Creatinine

Creatinine Clearance (X60 for mL/min)

$Cl_{Cr} \text{ ♂} = \frac{140 - \text{age(yrs)} \times \text{TBW (kg)}}{50 \times Cr_{\text{Serum}} (\mu\text{mol/L})}$

(mL/sec)

$Cl_{Cr} \text{ ♀ (mL/sec)} = Cl_{Cr} \text{ ♂} \times 0.85$

GUIDELINE

See the CCNS website

www.cancercare.ns.ca for the
guideline on Paclitaxel for ovarian
cancer

PATIENT VISIT

CHEMOTHERAPY VISIT:

Approx. 6 hours OR- Approx 4 1/2 hours
if concurrent

GY

GY-TOPOTEC

Topotecan Chemotherapy (Ovarian Cancer- Palliative Treatment)

INTERMEDIATE LEVEL REGIMEN-
Community Hospital with Oncology
Nurses

TOPOTECAN 1.25mg/m² IV Days 1 to 5 (Round to nearest 0.1mg)

- Mix in 50-100mL minibag (5% Dextrose or Normal Saline); Infuse over 30 minutes
- Final concentration should be 10mcg-500mcg/mL

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: INTERMEDIATE RISK

Pre-Chemotherapy (on Days 1 to 5)-

- Dexamethasone 8 mg PO; **AND/OR**
- Dopamine Receptor Antagonist PO (Metoclopramide 10mg PO; **OR** Prochlorperazine 10mg PO)

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses; **AND/OR**
- Dopamine Receptor Antagonist PO (Metoclopramide 10mgPO q4-6h PRN; **OR** Prochlorperazine 10mg PO q4-6h PRN)

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Renal failure (Suggested action)

1. If CrCl = 20-40 mL/min, **reduce** to 50% dose of Topotecan
2. If CrCl < 20 mL/min, **OMIT** dose of Topotecan

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Baseline renal function tests (if failure suspected) [serum creatinine, electrolytes & BUN]

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

GUIDELINE

See the CCNS website
www.cancercare.ns.ca for the
guideline on Topotecan for ovarian
cancer

PATIENT VISIT

CHEMOTHERAPY VISIT: Approx. 20
minutes

REGIMEN CONTENTS

HN-CISP-FC - Cisplatin Concurrent
Chemoradiotherapy Followed by 5-
Fluorouracil Infusion/Cisplatin 386

HN-FU-CISP - 5-Fluorouracil Infusion/
Cisplatin 388

HN-METHO - Methotrexate
Chemotherapy 390

HN-CISP-FC

Cisplatin Concurrent Chemoradiotherapy Followed by 5-Fluorouracil Infusion/Cisplatin Chemotherapy

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

(Combined Modality: Carcinoma of Nasopharynx)

PREHYDRATION

- Encourage patient to drink 6-8 glasses of water prior to chemo each day
- 2000mL Normal Saline with 20mEq/L Potassium Chloride; Infuse over 2 hours

CISPLATIN 100mg/m² IV Days 1, 22 & 43 (Round to nearest 1mg)

- Mix drug in 500mL Normal Saline; Infuse over 60 minutes
- May give 250mL of 20% Mannitol solution (50G); Infuse through sidearm concurrent with Cisplatin

POSTHYDRATION

- 1000mL Normal Saline (with 10mEq PotassiumChloride); Infuse over 1 hour (increase fluids if poor oral intake)

EVERY 21 DAYS DURING RADIOTHERAPY,

THEN GIVE

5-FLUOROURACIL 1000mg/m²/day CIV for 96 hours Starting on Day 1

- Continuous infusion using ambulatory infusion pump (Round to nearest 50mg- Maximum 2g/day)

PREHYDRATION

- Encourage patient to drink 6-8 glasses of water prior to chemo each day
- 2000mL Normal Saline with 20mEq/L Potassium Chloride; Infuse over 2 hours

CISPLATIN 80mg/m² IV Day 1 (Round to nearest 1mg- Maximum dose=150mg)

- Mix drug in 500mL Normal Saline; Infuse over 60 minutes
- May give 250mL of 20% Mannitol solution (50G); Infuse through sidearm concurrent with Cisplatin

POSTHYDRATION

- 1000mL Normal Saline (with 10mEq PotassiumChloride); Infuse over 1 hour (increase fluids if poor oral intake)

REPEAT EVERY 28 DAYS- 3 Cycles

DOSE MODIFICATION

Hematologic Toxicities:

1. If ANC <1.5 x 10⁹/L OR if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Gastrointestinal Toxicities:

1. If Mucositis or Diarrhea ≥ Grade 3 in previous course, **REDUCE** to 50% dose of 5-FU

Renal failure

1. If Renal Function has not returned to normal (CrCl > 60mL/min or Serum Creatinine <136μmol/L) by Day 1 of cycle, **DISCONTINUE CISPLATIN** (Recommended action)

Continued Next Page...

HN-CISP-FC

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO/IV (Ondansetron 8mg IV, OR Granisetron 1mg IV, OR Dolasetron 100mg IV), **AND**
- Dexamethasone 20mg IV **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses. **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) **When available in Canada**
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)
- *Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration*

CLINICAL MONITORING

- Serum creatinine and electrolytes (including Mg²⁺) before each treatment cycle and on Day 3 of each cycle
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Skin assessment**, especially extremities
- Baseline and **routine renal function tests**- especially if there are other concurrent nephrotoxic drugs

HEARING

0. No change
1. Asymptomatic
2. Tinnitus
3. Correctable hearing loss
4. Deafness

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss; moderate paraesthesia
3. Sensory loss interferes with function

Rated at each clinic visit

PATIENT VISIT

CHEMOTHERAPY VISIT: 4 to 6 hours
(depending on hydration)

HN-FU-CISP

5-Fluorouracil Infusion/ Cisplatin Chemotherapy

(Combined Modality or Salvage
Therapy: Head & Neck Carcinoma)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

PREHYDRATION

- Encourage patient to drink 6-8 glasses of water prior to chemo each day
- 2000mL Normal Saline with 20mEq/L Potassium Chloride; Infuse over 2 hours

CISPLATIN 80mg/m² IV Day 1 (Round to nearest 1mg)

- Mix drug in 500mL Normal Saline; Infuse over 60 minutes
- May give 250mL of 20% Mannitol solution (50G); Infuse through sidearm concurrent with Cisplatin

POSTHYDRATION:

- 1000mL Normal Saline (with 10mEq Potassium Chloride); Infuse over 1 hour (increase fluids if poor oral intake)

5-FLUOROURACIL 1000mg/m²/day CIV for 96 hours Starting on Day 1

- Admix in 1000mL Normal Saline and administer by Continuous Infusion over 96 hours (*Inpatient treatment*)
- Continuous infusion using ambulatory infusion pump (*Outpatient treatment*) (Round to nearest 50mg- Maximum 2g/day)

During **WEEKS 1 & 5 of Radiotherapy**; then **REPEAT EVERY 28 DAYS**

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy:

- Serotonin Receptor Antagonist PO/IV (Ondansetron 8mg IV, OR Granisetron 1mg IV, OR Dolasetron 100mg IV), **AND**
- Dexamethasone 20mg IV **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy:

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *When available in Canada*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)
- Oral hydration is strongly encouraged: poorly hydrated patients may need more IV hydration

HN-FU-CISP

CLINICAL MONITORING

- Serum creatinine and electrolytes (including Mg^{++}) before each treatment cycle and on Day 3 of each cycle
- Clinical assessment of stomatitis, oral examination upon patient complaint of a sore mouth
- **Skin assessment**, especially extremities
- Baseline and **routine renal function tests**- especially if there are other concurrent nephrotoxic drugs

HEARING

0 No change

1 Asymptomatic

2 Tinnitus

3 Correctable hearing loss

4 Deafness

SENSORY

0 No change

1 Mild paraesthesia; no deep tendon reflex

2 Mild/moderate sensory loss/moderate

paraesthesia

3 Sensory loss interferes with function

Rated at each clinic visit

DOSE MODIFICATION

Hematologic Toxicities

- 1 If ANC $< 1.5 \times 10^9/L$ OR if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Gastrointestinal Toxicities

1. If Mucositis or Diarrhea $\geq$ Grade 3 in previous course, **REDUCE** to 50% dose of 5-FU

Renal failure

1. If Renal Function has not returned to normal ($CrCl > 1.0 mL/sec$ or Serum Creatinine $< 136 \mu mol/L$) by Day 1 of cycle, **DISCONTINUE CISPLATIN**

(Recommended action)

PATIENT VISIT

CHEMOTHERAPY VISITS

Day 1 = 4 to 6 hours

Days 2 to 5 = 15 to 30 minutes

HN

HN-METHO

Methotrexate Chemotherapy

(Carcinoma- Head & Neck)

BASIC LEVEL REGIMEN-

Community Hospital with
Oncology Nurses

METHOTREXATE 40mg/m² IV Day 1 (Round to nearest 5mg)

- Slow push through sidearm of free flowing IV

REPEAT EVERY 7 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

- No routine antiemetic before chemotherapy
- After chemotherapy, use Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10mg PO q3-4h PRN

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Renal failure

1. If CrCl = 12-48mL/min or Serum Creatinine = 100-180µmol/L, reduce Methotrexate to **50%** dose
2. If CrCl < 12mL/min or Serum Creatinine > 180µmol/L, **Omit** Methotrexate dose (*Suggested action*)

Hepatic dysfunction

1. If Bilirubin = 50-85µmol/L or AST > 180IU/L, reduce Methotrexate to **75%** dose

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Clinical assessment of stomatitis: oral examination upon patient complaint of a sore mouth
- Baseline renal function tests (if failure suspected) [serum creatinine, electrolytes & BUN]

PATIENT VISIT

CHEMOTHERAPY VISIT

Approximately 30 minutes

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NOTE: Regimen names in *italics* are not in this pocketbook version- See full version for regimen monograph

LE-CHLORAM

Chlorambucil* PO Chemotherapy

Take-Home Prescription-
Unrestricted

(Chronic Lymphocytic Leukemia (Active or Indolent Disease)- Palliative Intent)

CHLORAMBUCIL 40 mg/m² PO Day 1

OR 8mg/m² PO daily for 14 days OR 4-10mg PO daily for 21 days

OR 3 to 6mg/m² PO daily until WBC < 10 x 10⁹/L, then 1 to 2mg/m² PO daily

(Outpatient prescription in multiples of 2mg tablets) (dosage may vary)

May also add:

PREDNISONE 50 mg PO daily for 5 to 10 days (dosage may vary)

(Outpatient prescription in multiples of 5mg and 50mg tablets)

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic before chemotherapy
- After chemotherapy, use
Prochlorperazine 10mg PO q4-6h
PRN, or Metoclopramide 10mg PO
q3-4h PRN

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.0 x 10⁹/L, or if Platelets < 100 x 10⁹/L, **HOLD** dose for 1 week

Hepatic dysfunction (Suggested action)

1. Consider dose reduction if LFTs elevated (eg Bilirubin or AST)

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum uric acid levels before each cycle of treatment
- Clinical pulmonary exam at each visit, incl. auscultation, pulmonary toxicity ratings

SHORT OF BREATH

0. No change
1. Mild SOB
2. Dyspnea on exertion
3. Dyspnea at normal level of activity
4. Dyspnea at rest

Rated at periodic clinic visits, at each visit after 6 months' treatment, or upon patient complaint

LE-CLAD* CIV

Cladribine Chemotherapy

(Hairy Cell Leukemia- Curative Intent)

ADVANCED LEVEL REGIMEN-

Provincial Cancer Centre

INTERMEDIATE LEVEL REGIMEN-

Regional Hospital with

Hematologist Supervision

CLADRIBINE 0.09 mg/Kg/day CIV for 7 days

- Continuous infusion using ambulatory infusion pump (Round to nearest 0.01mg)
- Admix in sufficient diluent (Normal Saline) to provide an infusion rate of 250mL/24hr
- Infuse through patent peripheral or central venous catheter; Inspect peripheral infusion sites daily and replace if evidence of irritation or extravasation

SINGLE COURSE ONLY

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic before chemotherapy
- After chemotherapy, use Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10mg PO q3-4h PRN

OTHER SUPPORTIVE CARE

- Cotrimoxazole DS 1 tablet daily on Saturday and Sunday (prophylaxis for PCP infection)

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Watch for symptoms of fever or infection

PHYSICIAN'S STANDING ORDERS AVAILABLE FOR THIS REGIMEN

PATIENT VISIT

CHEMOTHERAPY VISITS:

Day 1 = Approximately 30 minutes
Days 3, 5 & 8 = 15 to 30 minutes
Schedule pump teaching session
BEFORE first day

LE

Cyclophosphamide IV- Vincristine-Prednisone (CVP*IV) Chemotherapy

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

(Chronic Lymphocytic Leukemia- Palliative Intent)

VINCRIStINE 1.4 mg/m² IV Day 1 (Round to nearest 0.1mg)

• Push through sidearm of free flowing IV; Inject over at least 1 minute

CYCLOPHOSPHAMIDE 750 mg/m² IV Day 1 (Round to nearest 10mg)

• Mix in 250mL bag (Normal Saline); Infuse over 20-30 minutes

PREDNISONE 100 mg PO for 5 days

(Outpatient prescription in multiples of 50mg tablets)

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

Pre-Chemotherapy-

- Dopamine Receptor Antagonist PO
(e.g. Metoclopramide 10-20mg PO,
or Prochlorperazine 10mg PO)

Post-Chemotherapy-

- Prochlorperazine 10mg PO q4-6h
PRN, or Metoclopramide 10mgPO
q3-4h PRN

OTHER SUPPORTIVE CARE

- Oral hydration is strongly
encouraged, poorly hydrated
patients may need more IV
hydration (to prevent renal toxicity)

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.0 x 10⁹/L, or if Platelets
<100 x 10⁹/L, **HOLD** dose for 1
week

Hepatic dysfunction (Suggested action)

1. If Bili = 25-50µmol/L or AST = 60-
180IU/L, reduce Vincristine to **50%**
dose
2. If Bili = 51-85µmol/L or AST>
180IU/L, reduce Vincristine to **25%**
dose & Cyclophosphamide to **75%**
dose
3. If Bili > 85µmol/L, **Omit**
Cyclophosphamide & Vincristine

CLINICAL MONITORING

- Complete blood count including
differential, platelets and
hemoglobin (CBC) and serum
electrolytes before each cycle of
treatment
- Baseline renal function tests (if
failure suspected) [serum creatinine,
electrolytes & BUN]
- Serum glucose levels (monitor
routinely for diabetic patients)
- Periodic urinalysis (RBCs), Cystitis
toxicity ratings in response to patient
complaint
- Neurologic toxicity ratings
(Sensory, Constipation) at each visit

SENSORY

- 0 No change
- 1 Mild paraesthesia; no deep tendon
reflex
- 2 Mild/moderate sensory loss,
moderate paraesthesia
- 3 Sensory loss interferes with
function

CONSTIPATION

- 0 No change
- 1 Mild
- 2 Moderate
- 3 Severe
- 4 Ileus >96 hours

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

PATIENT VISIT
CHEMOTHERAPY VISIT:
Approximately 30-45 minutes

[Rev 11/01]

**Cyclophosphamide PO-
Vincristine-Prednisone
(CVP*PO) Chemotherapy**

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

(Chronic Lymphocytic Leukemia- Palliative Intent)

VINCRIStINE 1.2 mg/m² IV Day 1

(Round to nearest 0.1mg- To a maximum dose of 2mg)

- Push through sidearm of free flowing IV, Inject over at least 1 minute

CYCLOPHOSPHAMIDE 300 to 450 mg PO for 5 days

(Outpatient prescription in multiples of 25mg & 50mg tablets)

PREDNISONE 75 to 150 mg PO for 5 days

(dose may be tapered down after 5 days) (Outpatient prescription in multiples of 50mg tablets)

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic before chemotherapy
- After chemotherapy, use Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10mgPO q3-4h

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.0 x 10⁹/L, or if Platelets < 100 x 10⁹/L, **HOLD** dose for 1 week

Hepatic dysfunction (Suggested action)

1. If Bili = 25-50µmol/L or AST = 60-180IU/L, reduce Vincristine to **50%** dose
2. If Bili = 51-85µmol/L or AST > 180IU/L, reduce Vincristine to **25%** dose & Cyclophosphamide to **75%** dose
3. If Bili > 85µmol/L, **Omit** Cyclophosphamide & Vincristine

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

PATIENT VISIT

CHEMOTHERAPY VISIT:

Approximately 20-30 minutes

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes before each cycle of treatment
- Baseline renal function tests (if failure suspected) [serum creatinine, electrolytes & BUN]
- Serum glucose levels (monitor routinely for diabetic patients)
- Periodic urinalysis (RBCs), Cystitis toxicity ratings in response to patient complaint
- Neurologic toxicity ratings (Sensory, Constipation) at each visit

SENSORY

0. No change
1. Mild paraesthesia, no deep tendon reflex
2. Mild/moderate sensory loss, moderate paraesthesia
3. Sensory loss interferes with function

CONSTIPATION

0. No change
1. Mild
2. Moderate
3. Severe
4. Ileus >96 hours

LE

LE-CYTAR*HD

High Dose Cytarabine A.M.L. Consolidation Chemotherapy

ADVANCED LEVEL REGIMEN-
Hematology Inpatient Service

(Acute Myelogenous Leukemia- Post-Remission Consolidation)

CYTARABINE 3000 mg/m² IV q12h Days 1 to 6

(Total = 36,000mg/12 doses)

• Mix in 250mL Normal Saline; Infuse over 2 hours

**REPEAT EVERY 21 TO 28 DAYS-UPON HEMATOLOGIC
RECOVERY**

For a Usual Total of 2 Consolidation Cycles

SUPPORTIVE CARE

**ANTIEMETIC LEVEL INTERMEDIATE
RISK**

Pre-Chemotherapy-

- Dexamethasone 4-8 mg PO, and/or
- Dopamine Receptor Antagonist PO
(e.g. Metoclopramide 10-20mg PO,
or Prochlorperazine 10mg PO)

Post-Chemotherapy-

- Prochlorperazine 10mg PO q4-6h
PRN, or Metoclopramide 10mg PO
q3-4h PRN

OTHER SUPPORTIVE CARE

- Allopurinol 300mg PO qd for 8 days,
starting Day 0
- Prednisone Acetate 1% Eye Drops

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

CLINICAL MONITORING

- Complete blood count including
differential, platelets and
hemoglobin (CBC) and serum
uric acid levels before each cycle
of treatment
- Baseline & periodic liver function
tests (serum alkaline phosphatase,
GGT, ALT, AST & Bilirubin levels-
serum proteins may be added if
indicated)
- Baseline renal function tests (if
failure suspected) [serum creatinine,
electrolytes & BUN]
- Close neurological and systemic
monitoring of all organs (before
each dose) while drug is
administered in hospital
- Clinical pulmonary exam at each
visit, incl. auscultation, pulmonary
toxicity ratings (especially within the
first month after treatment)
- Cerebellar Neurotoxicity
Assessment Tool and sensory
toxicity ratings each visit, for the
first few weeks after treatment

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon
reflex
2. Mild/moderate sensory loss;
moderate paraesthesia
3. Sensory loss interferes with
function

Rated at each clinic visit

Continued Next Page...

LE-CYTAR*HD

DOSE MODIFICATION

Cerebellar Neurotoxicities

1. Complete Cerebellar Neurotoxicity Assessment Tool before each dose of high dose Cytarabine; If ANY Score ≥ 1 **HOLD** dose and notify Hematologist immediately

CEREBELLAR NEUROTOXICITY ASSESSMENT

	Score= 0	Score= 1
Level of Consciousness	Alert, easily aroused	Confused or somnolent
Speech Pattern	Clear	Slurred or confused
Nystagmus	No beats present	Rhythmic beats present
Gait	Steady	Unsteady
Romberg Test	Steady	Unsteady, loss of balance
Tremors	Absent	Present
Upper RAMs	Smoothly	Clumsy, awkward
Point to Point	Smoothly	Clumsy, awkward
Lower RAMs	Smoothly	Clumsy, awkward
Heel to Toe	Smoothly	Clumsy, awkward

Assessment Key

Tandem Walking, walk heel to toe in a straight line

Romberg Test, stand with feet together, without support from arms, test for steadiness with eyes open and shut

Arm Tremors, sit on bed, hold arms straight out with palms up

Upper RAMs (Rapid Alternating Movements), tap hand on thigh alternating between dorsal and palmar surface as fast as possible

Point-to-Point Test, touch finger to nose, repeat with finger further away each time

Lower RAMs, tap hand of testor with foot of patient as fast as possible

Heel to Toe, run heel down shin of opposite leg

PATIENT VISIT

CHEMOTHERAPY VISIT

Inpatient Treatments

LE-FLUDAR

Fludarabine Chemotherapy

(Chronic Lymphocytic Leukemia-
Palliative Intent)

BASIC LEVEL REGIMEN-

Community Hospital with Oncology
Nurses

FLUDARABINE 25 mg/m² IV Days 1 to 5 (Round to nearest 2.5mg)

• Mix in 50mL minibag (Normal Saline); Infuse over 15-30 minutes

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- Prochlorperazine 10mg PO (&/or PR) q4-6h PRN **OR**
- Dexamethasone 4-8mg PO q6-12h PRN for 1 to 5 days **OR BOTH**

OTHER SUPPORTIVE CARE

- Cotrimoxazole DS 1 tablet daily on each Saturday and Sunday (prophylaxis for PCP infection)

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.0 x 10⁹/L, or if Platelets < 100 x 10⁹/L, **HOLD** dose for 1 week

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum uric acid levels before each cycle of treatment
- Periodic clinical pulmonary exam, including auscultation, pulmonary toxicity ratings
- Watch for symptoms of fever or infection

SHORT OF BREATH

0. No change
1. Mild Shortness of Breath
2. Dyspnea on exertion
3. Dyspnea at normal level of activity
4. Dyspnea at rest

Rated at periodic clinic visits and in response to patient complaints

NOTE

ALWAYS use irradiated blood products after Fludarabine given

PATIENT VISIT

CHEMOTHERAPY VISIT:

Approximately 30-45 minutes

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

Fludarabine Oral

Chemotherapy

(Chronic Lymphocytic Leukemia-
Palliative Intent)

**Take-Home Prescription- Special
Authorization Required**

FLUDARABINE 40 mg/m² PO Days 1 to 5 (Round to nearest 2.5mg)

(Outpatient prescription in multiples of 10mg tablets)

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- Prochlorperazine 10mg PO (&/or PR) q4-6h PRN OR
- Dexamethasone 4-8mg PO q6-12h PRN for 1 to 5 days OR BOTH

OTHER SUPPORTIVE CARE

- Cotrimoxazole DS 1 tablet daily on each Saturday and Sunday (prophylaxis for PCP infection)

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.0 x 10⁹/L, or if Platelets < 100 x 10⁹/L, **HOLD** dose for 1 week

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum uric acid levels before each cycle of treatment
- Periodic clinical pulmonary exam, including auscultation, pulmonary toxicity ratings
- Watch for symptoms of fever or infection

SHORT OF BREATH

- 0 No change
1. Mild Shortness of Breath
2. Dyspnea on exertion
3. Dyspnea at normal level of activity
4. Dyspnea at rest

Rated at periodic clinic visits and in response to patient complaints

NOTE

- Prescription costs covered by most third party prescription plans
- *Pharmicare patients will require a physician letter, requesting approval for coverage*
- **ALWAYS** use irradiated blood products after Fludarabine given

LE-HYDROXYU**Hydroxyurea Chemotherapy***(Chronic Myelogenous Leukemia)***Take-Home Prescription-
Unrestricted****HYDROXYUREA 500-3000 mg/m² PO daily**

- Titrate dose as needed to reduce WBC to $10 \times 10^9/L$ or lower, or as tolerated
- When WBC in acceptable range, reduce or maintain dose (Outpatient prescription in multiples of 500mg capsules)
- Begin full dose treatment when WBC $> 50 \times 10^9/L$, titrate to lower dose or hold treatment when WBC $< 10 \times 10^9/L$
- Discontinue if disease enters accelerated phase; treat as ALL or AML (depending on the transformation phenotype)

CONTINUOUS TREATMENT TO RESPONSE**SUPPORTIVE CARE****ANTIEMETIC REGIMEN: LOW RISK**

- Prochlorperazine 10mg PO (and/or PR) q4-6h PRN OR Dexamethasone 4-8mg POq6-12h PRN for 1 to 5 days OR **Both**

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum uric acid levels before each cycle of treatment

DOSE MODIFICATION**Renal Failure (*Suggested Action*)**

1. Consider Dose Reduction if renal function is reduced (e.g. reduced Creatinine Clearance or Serum Creatinine)

LE-IDA-CYTAR*3&7

Idarubicin-Cytarabine A.M.L. Induction/Consolidation Treatment

(Acute Non-Lymphocytic Leukemia-
Curative Intent)

ADVANCED LEVEL REGIMEN-
Provincial Cancer Centre

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with
Hematologist Supervision

IDARUBICIN 12mg/m²/day IV for 3 days on Days 1 to 3

- Slow push through sidearm of free flowing IV over at least 1-5 minutes
- May be given via Ambulatory Infusion Pump; Admix to appropriate volume in Normal Saline and infuse over 3 days via disposable pump or via continuous infusion using CADD infusion pump

CYTARABINE 100mg/m²/day CIV for 7 days via Ambulatory Infusion Pump

- Admix to appropriate volume in Normal Saline and infuse over 7 days via disposable pump or via continuous infusion using CADD infusion pump
- Infuse through central venous access device; Separate cassettes and lines

REPEAT EVERY 21 TO 28 DAYS-UPON HEMATOLOGIC RECOVERY

For a Usual Total of of 1 or more Induction Cycles, followed by 2
Consolidation Cycles

SUPPORTIVE CARE

ANTIEMETIC LEVEL INTERMEDIATE RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO prechemo each day (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV- pre-chemo & 8mg PO qhs on Days 1 to 3; OR Granisetron 2mg PO or 1mg IV prechemo each day; OR Dolasetron 100mg PO or 100mg IV). **AND**
- Dexamethasone 8mg PO prechemo each day

Post-Chemotherapy-

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses after last chemo treatment, or Granisetron 2mg PO q24h for 2 days, or Dolasetron 100mg PO q24h for 2 days). **AND**
- Dexamethasone 8mg PO q24h for 3 doses after last chemo treatment

OTHER SUPPORTIVE CARE

- Allopurinol 300mg PO qd for 8 days, starting Day 0
- Prednisone Acetate 1% Eye Drops

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) serum electrolytes, and serum uric acid levels before each cycle of treatment
- Clinical exam for symptoms of **Congestive Heart Failure**
- Periodic cardiac tests (Echocardiograms, angiography and/or WMS studies) for all patients with cardiac risk factors or patients at or above the threshold dose levels
- Baseline liver function tests (if liver failure suspected) (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated)

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

Continued Next Page...

LE-IDA-CYTAR*3&7**DOSE MODIFICATION****Hematologic Toxicities (Consolidation ONLY)**

1. If ANC $< 1.0 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, **HOLD** dose for 1 week (Until ANC $\geq 1.0 \times 10^9/L$)

Hepatic dysfunction (Suggested action)

1. If Bili = 26-51 $\mu\text{mol/L}$ or AST = 60-180 IU/L, **reduce** Idarubicin to **50%** dose
2. If Bili = 52-85 $\mu\text{mol/L}$ or AST > 180 IU/L, **reduce** Idarubicin to **25%** dose
3. If Bili > 85 $\mu\text{mol/L}$, **OMIT** ALL drugs

PATIENT VISIT**CHEMOTHERAPY VISITS**

Day 1 = Approx. 30 minutes

Days 4 & 8 = Approx. 15 to 30 minutes

LE-IMATINIB

Imatinib (Gleevec) Chemotherapy

Take-Home Prescription-
Special Authorization Required

(Chronic Myelogenous Leukemia-Accelerated Phase or Blast Phase; Chronic Phase First Line treatment or if Interferon relapsed or contraindicated)

Accelerated Phase or Blast Phase

IMATINIB 600mg PO daily

- May increase to 800mg PO daily, as tolerated (lack of adverse effects) for progressive disease or failure to achieve adequate hematologic response after 3 months' therapy
- Take with food and large glass of water

Chronic Phase

IMATINIB 400mg PO daily

- May increase to 600mg PO daily, as tolerated (lack of adverse effects) for progressive disease or failure to achieve adequate hematologic response after 3 months' therapy
- Take with food and large glass of water

(Outpatient prescription in multiples of 200 tablets)

CONTINUOUS TREATMENT

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10mg PO q3-4h PRN

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes before each month of treatment
- Baseline and routine (e.g. monthly) liver function tests [serum alkaline phosphatase, ALT, AST & Bilirubin levels (serum proteins may be added if indicated)]
- Baseline weight, and regular monitoring for signs of fluid retention (including pulmonary edema, pleural or pericardial effusions)

NOTE

- Prescription costs covered by most third party prescription plans
- *Pharmacare patients will require a physician letter, requesting approval for coverage*
- The cost per month of treatment can range from \$2,300 to \$3,500

DOSE MODIFICATION

Hepatic dysfunction If Bili > 3x ULN (upper limit of normal) [xxxμmol/L] or AST > 5x ULN [xxxIU/L] HOLD Imatinib, when Bili < 1.5x ULN and AST < 5x ULN resume Imatinib at reduced dosage

Hematologic Suppression

- In chronic phase CML, if ANC ≤ 1.0 x 10⁹/L and/or platelets ≤ 50 x 10⁹/L, Hold Imatinib (until ANC > 1.5 x 10⁹/L and platelets > 75 x 10⁹/L), then resume at reduced dosage (300-400mg)
- In accelerated phase CML, if ANC ≤ 0.5 x 10⁹/L and/or platelets ≤ 10 x 10⁹/L, check if cytopenia is related to the leukemia; if not, reduce Imatinib dose (400mg). If cytopenia persists for 2 weeks, reduce Imatinib dose further (300mg). If cytopenia persists for 4 weeks, Hold Imatinib (until ANC > 1 x 10⁹/L and platelets > 20 x 10⁹/L), then resume at reduced dosage (300mg)

GUIDELINE

See the CCNS Website
www.cancercare.ns.ca for the
guideline on the use of Imatinib

LE-IFN[®]CML

Interferon Chemotherapy

(Chronic Myelogenous Leukemia)

Take-Home Prescription-
Special Authorization Required

INTERFERON ALFA 5 MU/m² SC daily

- Titrate dose as needed to reduce WBC to $2-5 \times 10^9/L$, or dose as tolerated
- When WBC in acceptable range, reduce or maintain dose (Outpatient prescription in multiples of 3, 5 or 10MU vials)
- May be given as 1 MU SC daily for 2 weeks, then 3 MU SC daily for 2 weeks, then 6 MU SC daily for 2 weeks, then 9-10 MU SC daily, if full dose tolerated

CONTINUOUS TREATMENT TO RESPONSE

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: NOT APPLICABLE

- Routine prophylaxis of flu-like symptoms with Acetaminophen 325-500mg tablets 1 or 2 tablets before each dose (especially if this adverse effect occurs with early doses)

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes before each cycle of treatment
- Routine toxicity ratings of Flu-like Symptoms, Lethargy at follow-up visits

LETHARGY

- 0 None
- 1 Mild (Performance Status decrease by 1)
- 2 Moderate (Performance Status decrease by 2)
- 3 Severe (Performance Status decrease by 3)

FLU-LIKE SYMPTOMS

- 0 None
- 1 Mild
- 2 Moderate
- 3 Severe (Arthralgia, myalgia, diaphoresis, rigours/chills)

Rated at monthly/quarterly clinic visit

LE-IFN-CYTAR

Interferon-Cytarabine Maintenance Chemotherapy

Take-Home Prescription-
Special Authorization Required

(Chronic Myelogenous Leukemia- Maintenance Phase)

INTERFERON ALFA 5 MU/m² SC daily

(Outpatient prescription in multiples of 3, 5 or 10MU vials)

- May be given as 1 MU SC daily for 2 weeks, then 3 MU SC daily for 2 weeks, then 6 MU SC daily for 2 weeks, then 9-10 MU SC daily, if full dose tolerated

CYTARABINE 20 mg/m² SC daily for 10 days every 4 weeks

- May dispense as vials with diluent for preparation and administration in the home, or as prefilled syringes (up to 10 day supply at a time)

(Outpatient prescription in multiples of 100mg vials)

- Titrate doses of each drug as needed to maintain WBC to $10 \times 10^9/L$ or lower, or dose as tolerated
- Discontinue treatment if disease enters accelerated phase; treat as ALL or AML (depending on the transformation phenotype)

CONTINUOUS TREATMENT TO RESPONSE

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: NOT APPLICABLE

- Routine prophylaxis of flu-like symptoms with Acetaminophen 325-500mg tablets 1 or 2 tablets before each dose (especially if this adverse effect occurs with early doses)

DOSE MODIFICATION

Renal failure (Suggested action)

1. Consider dose reduction if renal function is reduced (eg. reduced Creatinine Clearance/ Serum Creatinine)

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes before each cycle of treatment
- Routine toxicity ratings of Flu-like Symptoms. Lethargy at follow-up visits

LETHARGY

0. None
1. Mild (Performance Status decrease by 1)
2. Moderate (Performance Status decrease by 2)
3. Severe (Performance Status decrease by 3)

FLU-LIKE SYMPTOMS

0. None
 1. Mild
 2. Moderate
 3. Severe
- (Arthralgia, myalgia, diaphoresis, rigors/chills)

Rated at monthly/quarterly clinic visit

EF

LE-IFN-HU

Interferon-Hydroxyurea Induction Chemotherapy

Take-Home Prescription-
Special Authorization Required

(Chronic Myelogenous Leukemia- Induction Phase)

INTERFERON ALFA 5 MU/m² SC daily

(Outpatient prescription in multiples of 3, 5 or 10MU vials)

- May be given as 1 MU SC daily for 2 weeks, then 3 MU SC daily for 2 weeks, then 6 MU SC daily for 2 weeks, then 9-10 MU SC daily, if full dose tolerated

HYDROXYUREA 50 mg/Kg PO daily

(Outpatient prescription in multiples of 500mg capsules)

- Titrate doses of each drug as needed to reduce WBC to $10 \times 10^9/L$ or lower, or dose as tolerated. When WBC in acceptable range, reduce or maintain dose
- Discontinue treatment if disease enters accelerated phase; treat as ALL or AML (depending on the transformation phenotype)

CONTINUOUS TREATMENT TO RESPONSE

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: NOT APPLICABLE

- Routine prophylaxis of flu-like symptoms with Acetaminophen 325-500mg tablets 1 or 2 tablets before each dose (especially if this adverse effect occurs with early doses)

DOSE MODIFICATION

Renal failure (Suggested action)

1. Consider dose reduction if renal function is reduced (eg. reduced Creatinine Clearance/ Serum Creatinine)

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes before each cycle of treatment
- Routine toxicity ratings of Flu-like Symptoms, Lethargy at follow-up visits

LETHARGY

0. None
1. Mild (Performance Status decrease by 1)
2. Moderate (Performance Status decrease by 2)
3. Severe (Performance Status decrease by 3)

FLU-LIKE SYMPTOMS

0. None
 1. Mild
 2. Moderate
 3. Severe
- (Arthralgia, myalgia, diaphoresis, rigours/chills)

Rated at monthly/quarterly clinic visit

**Methotrexate Intrathecal
Chemotherapy- A.L.L.
Consolidation**

ADVANCED LEVEL REGIMEN-
Provincial Cancer Centre

(Acute Lymphocytic Leukemia- Consolidation Treatment)

METHOTREXATE 12 mg INTRATHECAL Once or twice weekly for 6 doses (Administer concurrently with Maintenance Treatment)

- To be given as Intrathecal injection; use unpreserved solution or mix in unpreserved diluent using strict aseptic technique
- Patient may be instructed to lie flat for 1 hour after intrathecal injection
- Do not give Methotrexate oral tablets during weeks on intrathecal injections
- Routine prophylaxis of pneumocystis carinii with Cotrimoxazole 2 tablets for one to three days after each injection

REPEAT TWICE WEEKLY

CLINICAL MONITORING

- Schedule of IT doses may be modified according to physician availability. Initialization of IT chemotherapy should be deferred until stabilization of any coagulopathy and reduction of circulating platelet count
- Methotrexate IT doses are flat doses and are NOT adjusted for body surface area

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

PATIENT VISIT

CHEMOTHERAPY VISIT
Approximately 90 minutes

LE

**Methotrexate-Mercaptopurine
Chemotherapy- A.L.L.
Maintenance**
(Acute Lymphocytic Leukemia)
**Take-Home Prescription-
Unrestricted**
METHOTREXATE 15 mg/m² PO Day 1

(May increase dose to a maximum of 25mg/m²)

(Outpatient prescription in multiples of 2.5mg tablets)

HOLD Methotrexate tablets on weeks that Methotrexate Intrathecal injections are given

6-MERCAPTOPURINE 90 mg/m² PO daily for 7 days

(May increase dose to a maximum of 100-150mg)

(Outpatient prescription in multiples of 50mg tablets)

REPEAT EVERY 7 DAYS
SUPPORTIVE CARE
ANTIEMETIC LEVEL LOW RISK

- No routine antiemetics before or after chemotherapy

DOSE MODIFICATION
Hematologic Toxicities

1. If ANC < 1.0 x 10⁹/L, or if Platelets < 100 x 10⁹/L,

HOLD dose for 1 week

Renal failure

1. If CrCl = 0.2-0.8mL/sec or Serum Creatinine = 100-180μmol/L, reduce Methotrexate to **50%** dose
2. If CrCl < 0.2mL/sec or Serum Creatinine > 180μmol/L, **Omit** Methotrexate dose
3. Consider Mercaptopurine dose reduction if renal function is reduced (eg. reduced Creatinine Clearance/Serum Creatinine)
(Suggested action)

Hepatic dysfunction (Suggested action)

1. If Bili = 50-85μmol/L or AST > 180IU/L, reduce Methotrexate to **75%** dose
2. If Bili > 85μmol/L, **Omit** Methotrexate dose

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Clinical assessment of stomatitis: oral examination upon patient complaint of a sore mouth
- Baseline renal function tests (if failure suspected) [serum creatinine, electrolytes & BUN]

[Rev 11/01]

LE-TIC

Tretinoin → Idarubicin- Cytarabine (TIC) Chemotherapy

(Acute Promyelocytic Leukemia-
Curative Intent)

ADVANCED LEVEL REGIMEN-
Provincial Cancer Centre

**Take-Home Prescription
(Tretinoin)- Special
Authorization Required**

IDARUBICIN 12mg/m²/day IV for 3 days on Days 1 to 3

- Slow push through sidearm of free flowing IV over at least 1-5 minutes
- May be given via Ambulatory Infusion Pump; Admix to appropriate volume in Normal Saline and infuse over 3 days via disposable pump or via continuous infusion using CADD infusion pump

CYTARABINE 100mg/m² day CIV for 7 days via Ambulatory Infusion Pump

- Admix to appropriate volume in Normal Saline and infuse over 7 days via disposable pump or via continuous infusion using CADD infusion pump
- Infuse through central venous access device; Separate cassettes and lines (May add chemotherapy to Tretinoin if the WBC rises rapidly)

TRETINOIN 45mg/m² PO daily Until Remission

(May be given twice daily in divided doses) (Oral treatment in multiples of 10mg capsules)

Upon Complete Response, Immediately Followed by:

REPEAT WHEN WBC COUNT RETURNS TO NORMAL

For a Usual Total of 3 Cycles- 2 Consolidation Cycles Following Complete Response to First Cycle

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

INTERMEDIATE RISK (Idarubicin-Cytarabine Treatments)

Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO prechemo each day (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV- pre-chemo & 8mg PO qhs on Days 1 to 3, OR Granisetron 2mg PO or 1mg IV prechemo each day, OR Dolasetron 100mg PO or 100mg IV). **AND**
- Dexamethasone 8mg PO prechemo each day

Post-Chemotherapy-

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses after last chemo treatment, or Granisetron 2mg PO q24h for 2 days, or Dolasetron 100mg PO q24h for 2 days). **AND**
- Dexamethasone 8mg PO q24h for 3 doses after last chemo treatment

OTHER SUPPORTIVE CARE

- Allopurinol 600mg PO qd for 8 days, starting on Day 0
- Prednisone Acetate 1% Eye Drops

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

NOTE

TRETINOIN is also known as All-Trans Retinoic Acid or ATRA)

Continued Next Page...

CLINICAL MONITORING

Tretinoin Cycle(s)

- Rating for **symptoms of hypervitaminosis A syndrome** at each visit
- Monitor **coagulation profile, triglyceride and cholesterol levels and liver function tests** regularly

APL Retinoic Acid Syndrome (APL patients only)

- **Complete blood count** before and after each treatment-
hyperleukocytosis may be first sign
- Regular **assessment of pulmonary function & all organ functions**

HYPERVITAMINOSIS SYMPTOMS

0. No symptoms
1. Dry mouth, dry lips, dry skin, asymptomatic erythema; mild macular or papular rash
2. Dry eyes, need artificial tears; painful or pruritic dry skin or skin rash area(s); mild edema; mild bone pain
3. Severe dry eyes; generalized painful, pruritic or symptomatic skin rash; dry mouth and lips which interfere with eating; moderate edema or bone pain
4. Exfoliative dermatitis or ulcerative dermatitis; dry eyes requiring enucleation

Rated at each clinic visit

Chemotherapy Cycle(s)

- **Complete blood count** including differential, platelets and **hemoglobin (CBC)** serum electrolytes, and **serum uric acid levels** before each cycle of treatment
- Clinical exam for symptoms of **Congestive Heart Failure**
- Periodic **cardiac tests** (Echocardiograms, angiography and/or WMS studies) for all patients with cardiac risk factors or patients at or above the threshold dose levels
- Baseline **liver function tests** (if liver failure suspected) (serum alkaline phosphatase, ALT, AST & Bilirubin levels- serum proteins may be added if indicated)

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.0 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, **HOLD** dose for 1 week

Renal failure

1. If Serum Creatinine $> 265 \mu\text{mol/L}$, **reduce** Tretinoin to $25\text{mg}/\text{m}^2$ & Idarubicin to **50%** dose

Hepatic dysfunction (Suggested action)

1. If Bili = $26-51 \mu\text{mol/L}$ or AST = $60-180 \text{IU/L}$, **reduce** Idarubicin to **75%**
2. If Bili = $52-85 \mu\text{mol/L}$ or AST $> 180 \text{IU/L}$, **reduce** Tretinoin to $25\text{mg}/\text{m}^2$ & Idarubicin to **50%** dose
3. If Bili $> 85 \mu\text{mol/L}$, **Omit** Idarubicin dose

LE-TRETIN

Tretinoin Chemotherapy

(Acute Promyelocytic Leukemia-
Curative Intent)

SPECIALIZED LEVEL REGIMEN-

Capital Health Cancer Care
Program ONLY

OR Take-Home Prescription (Tretinoin)- Special

Authorization Required

TRETINOIN 45mg/m² PO daily Until Remission

(May be given twice daily in divided doses) (Oral treatment in multiples of
10mg capsules)

(TRETINOIN is also known as ALL TRANS RETINOIC ACID)

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic before chemotherapy
- After chemotherapy, use Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10mg PO q3-4h PRN

OTHER SUPPORTIVE CARE

- Allopurinol 600mg PO qd for 8 days, starting on Day 0

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.0 x 10⁹/L, or if Platelets < 100 x 10⁹/L, **HOLD** dose for 1 week

Renal failure

1. If Serum Creatinine > 265 µmol/L, **reduce** Tretinoin to 25mg/m²

Hepatic dysfunction (Suggested action)

1. If Bili= 52-85 µmol/L or AST > 180 IU/L, **reduce** Tretinoin to 25mg/m²

NOTE

TRETINOIN is also known as All-Trans Retinoic Acid or ATRA)

CLINICAL MONITORING

- Rating for **symptoms of hypervitaminosis A syndrome** at each visit
- Monitor **coagulation profile, triglyceride and cholesterol levels** and **liver function tests** regularly

APL Retinoic Acid Syndrome (APL patients only)

- **Complete blood count** before and after each treatment-hyperleukocytosis may be first sign
- Regular **assessment of pulmonary function & all organ functions**

HYPERVITAMINOSIS A SYMPTOMS

0. No symptoms

1. Dry mouth, dry lips, dry skin, asymptomatic erythema; mild macular or papular rash
2. Dry eyes, need artificial tears; painful or pruritic dry skin or skin rash area(s); mild edema; mild bone pain
3. Severe dry eyes; generalized painful, pruritic or symptomatic skin rash; dry mouth and lips which interfere with eating; moderate edema or bone pain
4. Exfoliative dermatitis or ulcerative dermatitis; dry eyes requiring enucleation

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NOTE: *Regimen names in italics are not in this pocketbook version- See full version for regimen monograph*

**Carboplatin-Docetaxel
Chemotherapy**

(Advanced Non-Small Cell Lung
Cancer)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

PREMEDICATIONS:

DEXAMETHASONE 8mg PO, 3 doses before chemotherapy (evening before, morning of and 1 hour before chemotherapy), then 8mg PO BID for 3 doses after chemotherapy

DOCETAXEL 75mg/m² IV Day 1 (Round to nearest 3mg)

- Mix in 250mL bag (5% Dextrose or Normal Saline) to a maximum concentration of 1.0-0.3mg/mL; Use non-PVC tubing; Infuse through main IV line over 1 hour

CARBOPLATIN AUC= 6 mg/mL/min IV Day 1 (Round to nearest 5mg)

- Mix in 250mL bag (5% Dextrose); Infuse over 30 minutes

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO prechemo each day (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV- pre-chemo & 8mg PO qhs on Days 1 to 3 **OR**
 - Granisetron 2mg PO or 1mg IV prechemo each day, **OR** Dolasetron 100mg PO or 100mg IV prechemo each day). **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO) *"When available in Canada"*

Post-Chemotherapy-

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo, **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *"When available in Canada"*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

Continued Next Page...

LU-CARBO-DOCE

CLINICAL MONITORING

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Liver function tests** at baseline and before each cycle of treatment [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]
- Baseline and periodic **renal function tests** [serum creatinine, electrolytes & BUN]; **serum creatinine** level before each cycle of chemotherapy
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Skin assessment** at each visit, including nails and infusion veins
- Monitor **fluid retention** at each visit

SKIN TOXICITY

0. None
1. Hyperpigmentation
2. Atrophy
3. Subcutaneous fibrosis
4. Desquamation, ulceration, or necrosis

NAIL CHANGES

0. Normal
1. Discolouration or ridging (Villonichia) or pitting
2. Partial or complete loss of nail(s) or pain in nailbeds
3. -
4. -

FLUID RETENTION

0. None
1. Mild peripheral edema
2. Pleural edema, outpatient management
3. Pleural edema, inpatient management
4. Intubation required

Rated at each clinic visit

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Hepatic dysfunction (Recommended action)

1. If AST or ALT $> 60 IU/L$ ($> 1.5X$ ULN) or if Alk Phos $> 300 IU/L$ ($> 2.5X$ ULN), **reduce** Docetaxel to **75%** dose
2. If AST or ALT $> 200 IU/L$ ($> 5X$ ULN) or if Alk Phos $> 600 IU/L$ ($> 5X$ ULN), **HOLD** Docetaxel dose and contact physician

ALTERNATE ADJUSTMENT

3. If LFTs $> 1.5x$ ULN or Bilirubin $> ULN$ ($> 26 \mu mol/L$) during treatment, **HOLD** Docetaxel dose for 3 weeks and re-test

ULN = upper limit of normal for lab value

Renal failure (Recommended action)

1. If Serum Creatinine $= 136-150 \mu mol/L$ or Creatinine Clearance $= 40-60 mL/min$, **reduce** Carboplatin dose by **1mg/mL/min** (or by **50mg/m²**)
2. If Serum Creatinine $= 151-180 \mu mol/L$ or Creatinine Clearance $= 20-40 mL/min$, **reduce** Carboplatin dose by **2mg/mL/min** (or by **100mg/m²**)
3. If Serum Creatinine $> 181 \mu mol/L$ or Creatinine Clearance $< 20 mL/min$, **OMIT** Carboplatin dose
(Recommended action)

Continued Next Page...

LU-CARBO-DOCE

NOTE

Calvert AUC Dosing Formula

DOSE (mg)=target AUC x (GFR + 25)

- GFR expressed as measured Creatinine clearance (mL/min) or estimated from serum Creatinine Creatinine Clearance (X60 for mL/min)

$$Cl_{cr} \text{ ♂ } = \frac{140 - \text{age (yrs)} \times TBW (kg)}{50 \times Cr_{\text{serum}} (\mu\text{mol/L})}$$

(mL/sec)

$$Cl_{cr} \text{ ♀ } (mL/sec) = Cl_{cr} \text{ ♂ } \times 0.85$$

PATIENT VISIT

CHEMOTHERAPY VISIT:

Approx. 2 hours/day

LU-CARBO-ETOP

Carboplatin-Etoposide Chemotherapy

(Small Cell Lung Cancer)

INTERMEDIATE LEVEL REGIMEN
Regional Hospital with Dedicated
Cancer Treatment Unit

ETOPOSIDE 100mg/m² IV Days 1 to 3 (Round to nearest 10mg)

- Premixed in 500mL bags of Normal Saline; connect piggyback to IV line; Infuse over 60 minutes; Adjust rate if blood pressure drops

CARBOPLATIN AUC= 6 mg/mL/min IV Day 1 (Round to nearest 5mg)

- Mix in 250mL bag (5% Dextrose); Infuse over 30 minutes

REPEAT EVERY 21 DAYS

(IF COMBINED WITH RADIATION, REPEAT EVERY 28 DAYS)

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO prechemo each day (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV- pre-chemo & 8mg PO qhs on Days 1 to 3 **OR**
 - Granisetron 2mg PO or 1mg IV prechemo each day; **OR** Dolasetron 100mg PO or 100mg IV prechemo each day). **AND**
- Dexamethasone 8mg PO prechemo each day (may increase to 20mg PO or IV). **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO) **When available in Canada**

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo. **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) **When available in Canada**
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

LU-CARBO-ETOP

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes before each cycle of treatment
- **Neurologic** toxicity ratings (Sensory) at each visit
- Baseline and periodic renal function tests [serum creatinine, electrolytes & BUN], serum creatinine level before each cycle of chemotherapy
- Clinical assessment of stomatitis, oral examination upon patient complaint of a sore mouth
- Baseline blood pressure at each treatment; monitor for hypotension

SENSORY

0 No change

- 1 Mild paraesthesia, no deep tendon reflex
- 2 Mild/moderate sensory loss, moderate paraesthesia
- 3 Sensory loss interferes with function

Rated at each clinic visit

NOTE

Calvert AUC Dosing Formula

DOSE (mg)=target AUC x (GFR + 25)

- GFR expressed as measured Creatinine clearance (mL/min) or estimated from serum Creatinine Creatinine Clearance (X60 for mL/min)

$$Cl_{\text{creatinine}} \text{ (mL/sec)} = \frac{140 - \text{age (yrs)}}{72} \times \frac{\text{TBW (kg)}}{Cr_{\text{serum}} \text{ (}\mu\text{mol/L)}}$$

$$Cl_{\text{creatinine}} \text{ (mL/sec)} = Cl_{\text{creatinine}} \text{ (mL/sec)} \times 0.85$$

DOSE MODIFICATION

Hematologic Toxicities

- 1 If ANC < 1.5 x 10⁹/L, notify physician and HOLD dose (Until ANC ≥ 1.5 x 10⁹/L)

Renal failure (Recommended action)

- 1 If Serum Creatinine=136-150μmol/L or Creatinine Clearance =40-60mL/min, **reduce** Carboplatin dose by **1mg/mL/min** (or by **50mg/m²** for BSA dosing)
- 2 If Serum Creatinine=151-180μmol/L or Creatinine Clearance =20-40mL/min, **reduce** Carboplatin dose by **2mg/mL/min** (or by **100mg/m²** for BSA dosing)
- 3 If Serum Creatinine >181μmol/L or Creatinine Clearance <20mL/min, **OMIT** Carboplatin dose

Hepatic dysfunction (Suggested action)

- 1 If Bilirubin=26-51μmol/L or AST=60-180IU/L, reduce Etoposide to **50%** dose
- 2 If Bilirubin= 52-85μmol/L, reduce Etoposide to **25%** dose

PATIENT VISIT

CHEMOTHERAPY VISIT

Approx. 2 hours/day

97

LU-CARBO-GEM

Carboplatin-Gemcitabine Chemotherapy

(Advanced Non-Small Cell Lung
Cancer)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

BASIC LEVEL REGIMEN
(Gemcitabine Only Days)-
Community Hospital

GEMCITABINE 1000mg/m² IV Days 1, 8 and 15

(Dosing schedule may be adjusted for myelosuppression in each patient)
(Round to nearest 20mg)

- Mix drug in 250mL bag (Normal Saline); Infuse over 30 minutes through free-flowing IV

CARBOPLATIN AUC= 6 mg/mL/min IV Day 1 (Round to nearest 5mg)

- Mix in 250mL bag (5% Dextrose); Infuse over 30 minutes

REPEAT EVERY 28 DAYS)

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK- Day 1

Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO prechemo each day (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV- pre-chemo & 8mg PO qhs on Days 1 to 3 OR
 - Granisetron 2mg PO or 1mg IV prechemo each day. OR Dolasetron 100mg PO or 100mg IV prechemo each day). **AND**
- Dexamethasone 8mg PO prechemo each day (may increase to 20mg PO or IV). **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses. **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days. or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *When available in Canada*

INTERMEDIATE RISK - Days 8 & 15

Pre-Chemotherapy-

- Dopamine Receptor Antagonist PO (Prochlorperazine 10mg PO or Metoclopramide 10mg PO)

Post-Chemotherapy-

- Dopamine Receptor Antagonist PO (Prochlorperazine 10mg PO q4h PRN. OR Metoclopramide 10mg PO q4h

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

Continued Next Page

LU-CARBO-GEM

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes (including Mg^{++}) before each cycle of treatment
- Neurologic toxicity ratings (Sensory) at each visit
- Baseline and periodic renal function tests [serum creatinine & BUN], hepatic function tests [AST/ALT, Bilirubin] before each cycle of chemotherapy
- Clinical assessment of stomatitis, oral examination upon patient complaint of a sore mouth
- Baseline blood pressure at each treatment, monitor for hypotension

SENSORY

0. No change
1. Mild paraesthesia, no deep tendon reflex
2. Mild/moderate sensory loss/moderate paraesthesia
3. Sensory loss interferes with function

NOTE

Calvert AUC Dosing Formula

DOSE (mg) = target AUC $\times$ (GFR + 25)

- GFR expressed as measured Creatinine clearance (mL/min) or estimated from serum Creatinine Creatinine Clearance (X60 for mL/min)

$$Cl_{\text{♂}} = \frac{140 - \text{age (yr)}}{72} \times \frac{\text{TBW (kg)}}{72} \times Cr_{\text{serum}} \quad \left(\frac{\text{mL/sec}}{50 \times Cr_{\text{serum}} (\mu\text{mol/L})} \right)$$

$$Cl_{\text{♀}} (\text{mL/sec}) = Cl_{\text{♂}} \times 0.85$$

DOSE MODIFICATION

Hematologic Toxicities

1. If $ANC < 1.5 \times 10^9/L$ OR if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose (Until $ANC \geq 1.5 \times 10^9/L$)

Renal failure (Recommended action)

1. If Serum Creatinine = 136-150 $\mu\text{mol/L}$ or Creatinine Clearance = 40-60 mL/min, **reduce** Carboplatin dose by **1mg/mL/min** (or by **50mg/m²** for BSA dosing)
2. If Serum Creatinine = 151-180 $\mu\text{mol/L}$ or Creatinine Clearance = 20-40 mL/min, **reduce** Carboplatin dose by **2mg/mL/min** (or by **100mg/m²** for BSA dosing)
3. If Serum Creatinine $> 181 \mu\text{mol/L}$ or Creatinine Clearance $< 20 \text{ mL/min}$, **OMIT** Carboplatin dose

Gastrointestinal Toxicities

1. If Mucositis or Diarrhea $\geq$ Grade 3 in previous course, **REDUCE** Gemcitabine to **50%** dose

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

PATIENT VISIT

CHEMOTHERAPY VISIT

Approx. 2 hours/day

LU

LU-CARBO-PACLI

Carboplatin-Paclitaxel Chemotherapy

(Advanced Non-Small Cell Lung
Cancer)

INTERMEDIATE LEVEL REGIMEN
Regional Hospital with Dedicated
Cancer Treatment Unit

PREMEDICATIONS:

DEXAMETHASONE 20mg PO 12 & 6 hours before Paclitaxel

OR- 20mg IV starting 45 minutes before Paclitaxel

DIPHENHYDRAMINE 50mg IV & RANITIDINE 50mg IV

- Admixed together in 50mL minibag of Normal Saline. Give over 15 minutes, starting 30 minutes before Paclitaxel

PACLITAXEL 225mg/m² IV Infuse over 3 hours Day 1

(Round to nearest 3mg)

- Mix in 500mL bag (5% Dextrose- dilution concentration 0.3-1.2 mg/mL); Use non-PVC equipment, including 0.22 micron in-line filter; Infuse over 3 hours
- Take a baseline blood pressure measurement, if prior hypotension

CARBOPLATIN AUC= 6 mg/mL/min IV Day 1 (Round to nearest 5mg)

- Mix in 250mL bag (5% Dextrose), Infuse over 30 minutes
- May infuse concurrently with Paclitaxel, using a Y-connector

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: INTERMEDIATE RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO, OR Granisetron 2mg PO, OR Dolasetron 100mg PO)

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses. **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- May give a Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO/ 10mg PR q4h PRN post chemo **OR** Metoclopramide 10mg PO q4-6h PRN post chemo)

OTHER SUPPORTIVE CARE

- Filgrastim 5mcg/kg SC daily (or 300mg total dose, 480mg for patients $\geq 100\text{Kg}$) may be started on Day 2, and continue for 6-10 days or until ANC $>1.5 \times 10^9/\text{L}$ for 2 consecutive days

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

Continued Next Page...

LU-CARBO-PACLI

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes (including Mg^{2+}) before each cycle of treatment
- Baseline and periodic renal function tests [serum creatinine, electrolytes & BUN], serum creatinine level before each cycle of chemotherapy
- Liver function tests [GGT, ALT, AST & Bilirubin levels] before each cycle of treatment
- Watch for symptoms of fever or infection
- Neurologic (Sensory), hypersensitivity and flu-like symptoms toxicity ratings at each visit
- Baseline blood pressure and pulse rate monitoring during drug administration & for the following hour

SENSORY

- 0 No change
- 1 Mild paraesthesia, no deep tendon reflex
- 2 Mild/moderate sensory loss; moderate paraesthesia
- 3 Sensory loss interferes with function

FLU-LIKE SYMPTOMS

(Arthralgia myalgia)

- 0 None
- 1 Mild
- 2 Moderate
- 3 Severe

HYPERSENSITIVITY/ALLERGY

- 0 None
- 1 Transient rash, fever $<38^{\circ}C$
- 2 Urticaria, fever $\geq 38^{\circ}C$, mild bronchospasm
- 3 Serum sickness, bronchospasm, requires parenteral meds
- 4 Anaphylaxis

Rated at each clinic visit

DOSE MODIFICATION

Hematologic Toxicities

1. If $ANC < 1.5 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Hepatic dysfunction (Suggested action)

1. If $Bili \geq 25 \mu mol/L$, give Paclitaxel maximum dose of $135 mg/m^2$
2. If $Bili = 26-51 \mu mol/L$ or $AST = 60-180 IU/L$, give Paclitaxel maximum dose of $75 mg/m^2$
3. If $Bili = 52-85 \mu mol/L$, give Paclitaxel maximum dose of $50 mg/m^2$

Renal failure (Recommended action)

1. If Serum Creatinine = $136-150 \mu mol/L$ or Creatinine Clearance = $40-60 mL/min$, **reduce** Carboplatin dose by $1 mg/mL/min$ (or by $50 mg/m^2$ for BSA dosing)
2. If Serum Creatinine = $151-180 \mu mol/L$ or Creatinine Clearance = $20-40 mL/min$, **reduce** Carboplatin dose by $2 mg/mL/min$ (or by $100 mg/m^2$ for BSA dosing)
3. If Serum Creatinine $> 181 \mu mol/L$ or Creatinine Clearance $< 20 mL/min$, **OMIT** Carboplatin dose

Continued Next Page...

LU-CARBO-PACLI

NOTE

Calvert AUC Dosing Formula

DOSE (mg)=target AUC x (GFR + 25)

• GFR expressed as measured

Creatinine clearance (mL/min) or

estimated from Serum Creatinine

Creatinine Clearance (X60 for mL/min)

$Cl_{cr} \text{ (mL/sec)} = \frac{140 - \text{age (yrs)} \times \text{TBW (kg)}}{50 \times Cr_{\text{serum}} (\mu\text{mol/L})}$

$Cl_{cr} \text{ (mL/sec)} = Cl_{cr} \text{ (mL/min)} \times 0.85$

$Cl_{cr} \text{ (mL/sec)} = Cl_{cr} \text{ (mL/min)} \times 0.85$

PATIENT VISIT

CHEMOTHERAPY VISIT

Approx. 6 hours OR- Approx 4 1/2 hours
if concurrent

LU-CARBO-VINOR

Cisplatin-Vinorelbine Chemotherapy

(Recurrent Metastatic Non-Small Cell
Lung Cancer)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

VINORELBINE 25mg/m² IV Days 1, 8, 15 & 22 (Round to nearest 1mg)

May reduce dose to 20mg/m² IV or omit Day 22 dose (if poorly tolerated)

- Slow push through sidearm of free flowing IV (Normal Saline 250mL);
Infuse over 6-10 minutes; infuse balance of IV bag
- If extravasation occurs during administration, discontinue immediately and
infuse the remaining dose through another IV site (into another vein)

CARBOPLATIN AUC= 6 mg/mL/min IV Day 1 (Round to nearest 5mg)

- Mix in 250mL bag (5% Dextrose); Infuse over 30 minutes

REPEAT EVERY 28 DAYS)

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

Cisplatin Day 1 - HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute
Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-
200mg PO or 100mg IV), **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV), **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if
given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron
given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for
1-2 days, if given pre-chemo, **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo
(Aprepitant 80 mg PO q 24 hours for 3 days) *When available in Canada*

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push
Vinorelbine Only Days - LOW RISK
- May give a Dopamine Receptor Antagonist (Prochlorperazine 10mg PO
prechemo, then q4-6h PRN, OR Metoclopramide 10mg PO prechemo, then
q4-6h PRN)

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

Continued Next Page...

LU-CARBO-VINOR

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes before each cycle of treatment
- Neurologic toxicity ratings (Sensory) at each visit
- Baseline and periodic renal function tests [serum creatinine, electrolytes & BUN]; serum creatinine level before each cycle of chemotherapy
- Baseline and periodic hepatic function tests [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels] before each cycle of chemotherapy
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth
- Baseline blood pressure at each treatment; monitor for hypotension

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss/moderate paraesthesia
3. Sensory loss interferes with function

Rated at each clinic visit

NOTE

Calvert AUC Dosing Formula

$$\text{DOSE (mg)} = \text{target AUC} \times (\text{GFR} + 25)$$

- GFR expressed as measured Creatinine clearance (mL/min) or estimated from serum Creatinine Creatinine Clearance (X60 for mL/min)

$$\text{Cl}_{\text{Cr}} \text{ ♂ (mL/sec)} = \frac{140 - \text{age (yrs)}}{50} \times \frac{\text{TBW (kg)}}{\text{Cr}_{\text{Serum}} (\mu\text{mol/L})}$$

$$\text{Cl}_{\text{Cr}} \text{ ♀ (mL/sec)} = \text{Cl}_{\text{Cr}} \text{ ♂} \times 0.85$$

DOSE MODIFICATION

Hematologic Toxicities

1. If $\text{ANC} < 1.5 \times 10^9/\text{L}$, notify physician and **HOLD** dose (Until $\text{ANC} \geq 1.5 \times 10^9/\text{L}$)

Renal failure (Recommended action)

1. If Serum Creatinine = 136-150 $\mu\text{mol/L}$ or Creatinine Clearance = 40-60 mL/min; **reduce** Carboplatin dose by **1mg/mL/min** (or by **50mg/m²** for BSA dosing)
2. If Serum Creatinine = 151-180 $\mu\text{mol/L}$ or Creatinine Clearance = 20-40 mL/min; **reduce** Carboplatin dose by **2mg/mL/min** (or by **100mg/m²** for BSA dosing)
3. If Serum Creatinine > 181 $\mu\text{mol/L}$ or Creatinine Clearance < 20 mL/min, **OMIT** Carboplatin dose

Hepatic dysfunction

1. If AST = 60-180 IU/L or Bili = 36-50 $\mu\text{mol/L}$, **reduce** Vinorelbine to **50%** dose
2. If AST > 180 IU/L or Bili > 50 $\mu\text{mol/L}$, **reduce** Vinorelbine to **25%** dose

PATIENT VISIT

CHEMOTHERAPY VISIT:

Carboplatin/Vinorelbine Days

Approximately 1 hour

Vinorelbine ONLY Days

Approximately 30 minutes

**Cyclophosphamide-Doxorubicin-
Vincristine (CAV) Chemotherapy**

(Small Cell Lung Cancer)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

PREHYDRATION

- Encourage patients to drink 6-8 glasses of water prior to chemo each day- especially Day 1 (increase fluids if poorly hydrated)
- May prehydrate with 500mL Normal Saline; Infuse over 60 minutes

DOXORUBICIN 50mg/m² IV Day 1 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV over at least 3-5 minutes
- Slow down injection rate if erythematous streaking occurs

VINCRIPTINE 1.4mg/m² IV Day 1

- Push through sidearm of free flowing IV; Inject over at least 1 minute

CYCLOPHOSPHAMIDE 1000mg/m² IV Day 1 (Round to nearest 10mg)

- Mix in 500mL bag (5% Dextrose or Normal Saline); Infuse over 90 minutes

POSTHYDRATION

- May give 500mL Normal Saline if additional hydration needed; Infuse over 60 minutes

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, OR Granisetron 2mg PO or 1mg IV, OR Dolasetron 100mg PO or 100mg IV), **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV), **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo, **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *When available in Canada*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration
- Inadequate total hydration may result in dose-related hemorrhagic cystitis

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

Continued Next Page...

LU-CAV

CLINICAL MONITORING

- **Complete blood count** including differential, platelets and hemoglobin (CBC) and **serum electrolytes** before each cycle of treatment
- **Liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels] before each cycle of treatment
- **Renal function tests** at baseline and before each cycle of treatment [serum creatinine & BUN]
- **Baseline cardiac tests** (MUGA scan) for all patients & periodic cardiac tests for patients with cardiac risk factors or patients at or above the threshold dose levels
- Clinical exam for symptoms of **Congestive Heart Failure**
- **Neurologic toxicity ratings** (Sensory, Constipation) at each visit
- **Urinalysis (RBCs)**- periodic and in response to patient complaint

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss; moderate paraesthesia
3. Sensory loss interferes with function

CONSTIPATION

0. No change
1. Mild
2. Moderate
3. Severe
4. Ileus >96 hours

Rated at each clinic visit

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < $1.5 \times 10^9/L$, or if Platelets < $100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week (Until ANC $\geq 1.5 \times 10^9/L$)

Renal failure

1. If Serum Creatinine > $265 \mu\text{mol/L}$, reduce Doxorubicin to **50%** dose
2. If Creatinine Clearance < 12mL/min, **OMIT** Cyclophosphamide dose (*Suggested action*)

Hepatic dysfunction

1. If Bili = $25-50 \mu\text{mol/L}$ or AST = $60-180 \text{ IU/L}$, reduce Doxorubicin and Vincristine to **50%** dose
2. If Bili = $51-85 \mu\text{mol/L}$ or AST > 180 IU/L , reduce Cyclophosphamide to **75%** dose, & Doxorubicin and Vincristine to **25%** dose
3. If Bili > $85 \mu\text{mol/L}$, **OMIT ALL** drugs (*Suggested action*)

NOTE

This regimen may be substituted for Cisplatin-Etoposide, for the treatment of Small Cell Lung Cancer patients.

PATIENT VISIT

CHEMOTHERAPY VISIT:

Approximately 2 hours

LU-CISP-DOCE

Cisplatin-Docetaxel

Chemotherapy

(Advanced Non-Small Cell Lung
Cancer)

INTERMEDIATE LEVEL REGIMEN-

Regional Hospital with Dedicated
Cancer Treatment Unit

PREMEDICATIONS:

DEXAMETHASONE 8mg PO, 3 doses before Docetaxel chemotherapy (evening before, morning of and 1 hour before chemotherapy), then 8mg PO BID for 5 doses after chemotherapy

PREHYDRATION

- Encourage patient to drink 6-8 glasses of water prior to chemo each day
- May give 1000mL Normal Saline; Infuse over 1 hour on Day 1

DOCETAXEL 75mg/m² IV Day 1 (Round to nearest 3mg)

- Mix in 250mL bag (5% Dextrose or Normal Saline) to a maximum concentration of 1.0-0.3mg/mL; Use non-PVC tubing; Infuse through main IV line over 1 hour

CISPLATIN 70mg/m² IV on Day 1 (Round to nearest 1mg)

- Mix drug in 500mL bag (Normal Saline); Infuse over 60 minutes; May also admix 20G Mannitol (200mL of 10% solution) with Cisplatin

POSTHYDRATION

- May give 1000mL Normal Saline (may add 10mEq/L Potassium Chloride and 8mmol/L Magnesium Sulphate); Infuse over 1 hour on Day 1

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist IV after hydration and before chemo (Ondansetron 8mg IV; OR Granisetron 1mg IV; OR Dolasetron 100mg IV),

AND

- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO) *"When available in Canada"*

Post-Chemotherapy-

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO/IV q12h for 3 doses if given prechemo) **OR**

- No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**

- Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo, **AND**

- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *"When available in Canada"*

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

PHYSICIAN'S STANDING ORDERS

AVAILABLE FOR THIS REGIMEN

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CLINICAL MONITORING

- **Complete blood count** including differential, platelets and hemoglobin (CBC) and **serum electrolytes** [including Mg^{2+}] before each cycle of treatment
- **Liver function tests** at baseline and before each cycle of treatment [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]
- Watch for symptoms of **fever or infection**
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Skin assessment** at each visit, including nails and infusion veins
- Monitor **fluid retention** at each visit
- **Renal function tests** [serum creatinine & BUN] checked before each cycle of chemotherapy
- **Hearing & Neurologic** toxicity ratings (Sensory)- each visit

HEARING

0. No change
1. Asymptomatic
2. Tinnitus
3. Correctable hearing loss
4. Deafness

SENSORY

0. No change
1. Mild paraesthesia, no deep tendon reflex
2. Mild/moderate sensory loss; moderate paraesthesia
3. Sensory loss interferes with function

SKIN TOXICITY

0. None
1. Hyperpigmentation
2. Atrophy
3. Subcutaneous fibrosis
4. Desquamation, ulceration, or necrosis

NAIL CHANGES

0. Normal
1. Discolouration or ridging (Vailonychia) or pitting
2. Partial or complete loss of nail(s) or pain in nailbeds
3. - 4 -

FLUID RETENTION

- 0 None
- 1 Mild peripheral edema
- 2 Pleural edema, outpatient management
- 3 Pleural edema, inpatient management
- 4 Intubation required

Rated at each clinic visit

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Hepatic dysfunction

1. If AST or ALT $> 60 IU/L$ ($> 1.5X$ ULN) or if Alk Phos $> 300 IU/L$ ($> 2.5X$ ULN), **reduce** to **75%** dose
2. If AST or ALT $> 200 IU/L$ ($> 5X$ ULN) or if Alk Phos $> 600 IU/L$ ($> 5X$ ULN), **HOLD** dose and contact physician

ALTERNATE ADJUSTMENT

3. If LFTs $> 1.5x$ ULN or Bilirubin $> ULN$ ($> 26 \mu mol/L$) during treatment, **HOLD** dose for 3 weeks and re-test

ULN = upper limit of normal for lab value

(Recommended action)

Renal failure (Recommended action)

1. If CrCl = 30-60 mL/min or Serum Creatinine = 136-185 $\mu mol/L$, reduce Cisplatin to **50%** dose
2. If CrCl $< 30 mL/min$ or Serum Creatinine $> 185 \mu mol/L$, **Omit** Cisplatin dose

PATIENT VISIT

CHEMOTHERAPY VISIT

Approx. 2 hours/day

27

LU-CISP-ETOP

Cisplatin-Etoposide Chemotherapy

(Small Cell Lung Cancer)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

PREHYDRATION

- Encourage patient to drink 6-8 glasses of water prior to chemo each day
- May prehydrate with 500mL Normal Saline; Infuse over 60 minutes Days 1 to 3

ETOPOSIDE 100mg/m² IV Days 1 to 3 (Round to nearest 10mg)

- Premixed in 500mL bags of Normal Saline; connect piggyback to IV line; Infuse over 60 minutes; Adjust rate if blood pressure drops
- Give Etoposide BEFORE Cisplatin, to hydrate patient

CISPLATIN 25mg/m² IV Days 1 to 3 (Round to nearest 1mg)

- Mix drug in 250mL bag (Normal Saline); Infuse over 60 minutes; May also admix 10G Mannitol (100mL of 10% solution) with Cisplatin

POSTHYDRATION

- May give 500mL Normal Saline if additional hydration needed; Infuse over 60 minutes Days 1-3

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO prechemo each day (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV- pre-chemo & 8mg PO qhs on Days 1 to 3 OR
 - Granisetron 2mg PO or 1mg IV prechemo each day; OR Dolasetron 100mg PO or 100mg IV prechemo each day). **AND**
- Dexamethasone 8mg PO prechemo each day (may increase to 20mg PO or IV). **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO) **When available in Canada**

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo. **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) **When available in Canada**
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

Continued Next Page...

LU-CISP-ETOP

CLINICAL MONITORING

- **Complete blood count** including differential, platelets and hemoglobin (CBC) and serum electrolytes [including Mg^{++}] before each cycle of treatment
- **Renal function tests** [serum creatinine & BUN] before each cycle of chemotherapy
- **Liver function** [Bilirubin levels] checked before each cycle of treatment
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Hearing & Neurologic toxicity** ratings (Sensory)- each visit

HEARING

0. No change
1. Asymptomatic
2. Tinnitus
3. Correctable hearing loss
4. Deafness

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss, moderate paraesthesia
3. Sensory loss interferes with function

Rated at each clinic visit

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

DOSE MODIFICATION

Hematologic Toxicities

1. If $ANC < 1.5 \times 10^9/L$ or if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose (Until $ANC \geq 1.5 \times 10^9/L$)

Renal failure (Recommended action)

1. If $CrCl = 30-60 mL/min$ or Serum Creatinine $= 136-185 \mu mol/L$, reduce Cisplatin to **50%** dose, and Etoposide to **75%** dose
2. If $CrCl < 30 mL/min$ or Serum Creatinine $> 185 \mu mol/L$, **Omit** Cisplatin dose
3. If $CrCl < 12 mL/min$, reduce Etoposide to **50%** dose

Hepatic dysfunction (Suggested action)

1. If $Bili = 26-51 \mu mol/L$ or $AST = 60-180 IU/L$, reduce Etoposide to **50%** dose
2. If $Bili = 52-85 \mu mol/L$, reduce Etoposide to **25%** dose
3. If $Bili > 85 \mu mol/L$ or $AST > 180 IU/L$, **Omit** Etoposide

NOTE

This is the regimen usually recommended for treatment of Small Cell Lung Cancer.

PATIENT VISIT

CHEMOTHERAPY VISIT

Approx. 2 hours/day

LU-CISP-ETOP*PAN

Cisplatin-Etoposide (Pancoast) Chemotherapy

(Pancoast Tumour - Lung Cancer)

INTERMEDIATE LEVEL REGIMEN
Regional Hospital with Dedicated
Cancer Treatment Unit

PREHYDRATION

- Encourage patient to drink 6-8 glasses of water prior to chemo each day
- May prehydrate with 500mL Normal Saline; Infuse over 60 minutes Days 1 and 8

ETOPOSIDE 50 mg/m² IV Days 1 to 5 (Round to nearest 10mg)

- Premixed in 500mL bags of Normal Saline; connect piggyback to IV line; Infuse over 60 minutes; Adjust rate if blood pressure drops
- Give Etoposide BEFORE Cisplatin, to hydrate patient

CISPLATIN 50 mg/m² IV Days 1 and 8 (Round to nearest 1mg)

- Mix drug in 250mL bag (Normal Saline); Infuse over 60 minutes. May also admix 20G Mannitol (200mL of 10% solution) with Cisplatin

POSTHYDRATION

- May give 500mL Normal Saline if additional hydration needed. Infuse over 60 minutes Days 1-3

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO prechemo each day (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV- pre-chemo & 8mg PO qhs on Days 1 to 3 OR
 - Granisetron 2mg PO or 1mg IV prechemo each day. OR Dolasetron 100mg PO or 100mg IV prechemo each day). AND
- Dexamethasone 8mg PO prechemo each day (may increase to 20mg PO or IV). AND
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO) *"When available in Canada"*

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses. AND
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) OR
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo OR
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo. AND
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *"When available in Canada"*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

Continued Next Page

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes [including Mg^{2+}] before each cycle of treatment
- Renal function tests [serum creatinine & BUN] before each cycle of chemotherapy
- Liver function [Bilirubin levels] checked before each cycle of treatment
- Clinical assessment of stomatitis, oral examination upon patient complaint of a sore mouth
- Hearing & Neurologic toxicity ratings (Sensory)- each visit

HEARING

- 0 No change
- 1 Asymptomatic
- 2 Tinnitus
- 3 Correctable hearing loss
- 4 Deafness

SENSORY

- 0 No change
- 1 Mild paraesthesia, no deep tendon reflex
- 2 Mild/moderate sensory loss, moderate paraesthesia
- 3 Sensory loss interferes with function

Rated at each clinic visit

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

DOSE MODIFICATION

Hematologic Toxicities

- 1. If $ANC < 1.5 \times 10^9/L$ or if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose (Until $ANC \geq 1.5 \times 10^9/L$)

Renal failure (Recommended action)

- 1. If $CrCl = 30-60 mL/min$ or Serum Creatinine $= 136-185 \mu mol/L$, reduce Cisplatin to **50%** dose, and Etoposide to **75%** dose
- 2. If $CrCl < 30 mL/min$ or Serum Creatinine $> 185 \mu mol/L$, **Omit** Cisplatin dose
- 3. If $CrCl < 12 mL/min$, reduce Etoposide to **50%** dose

Hepatic dysfunction (Suggested action)

- 1. If $Bili = 26-51 \mu mol/L$ or $AST = 60-180 IU/L$, reduce Etoposide to **50%** dose
- 2. If $Bili = 52-85 \mu mol/L$, reduce Etoposide to **25%** dose
- 3. If $Bili > 85 \mu mol/L$ or $AST > 180 IU/L$, **Omit** Etoposide

PATIENT VISIT

CHEMOTHERAPY VISIT

Approx. 2 hours/day

27

LU-CISP-GEM

Cisplatin-Gemcitabine Chemotherapy

(Advanced Non-Small Cell Lung
Cancer)

ADVANCED LEVEL REGIMEN-
Provincial Cancer Centre

BASIC LEVEL REGIMEN
(Gemcitabine Only Days)-
Community Hospital with
Oncology Nurses

PREHYDRATION

- Encourage patient to drink 6-8 glasses of water prior to chemo each day
- May give 1000mL Normal Saline; Infuse over 1 hour on Day 1

GEMCITABINE 1000mg/m² IV on Days 1, 8 & 15 (Round to nearest 20mg)
(Dosing schedule may be adjusted for myelosuppression in each patient)

- Mix drug in 250mL bag (Normal Saline); Infuse over 30 minutes through free-flowing IV

CISPLATIN 70mg/m² IV on Day 1 (Round to nearest 1mg)

- Mix drug in 500mL bag (Normal Saline); Infuse over 60 minutes; May also admix 20G Mannitol (200mL of 10% solution) with Cisplatin

POSTHYDRATION

- May give 1000mL Normal Saline (may add 10mEq/L Potassium Chloride and 8mmol/L Magnesium Sulphate); Infuse over 1 hour on Day 1

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

Day 1- HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist IV prechemo (Ondansetron 8mg IV, OR Granisetron 1mg IV, OR Dolasetron 100mg IV), **AND**
- Dexamethasone 20mg IV, **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO) *"When available in Canada"*

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
 - Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo, **AND**
 - Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *"When available in Canada"*
- Days 8 & 15- INTERMEDIATE RISK
- May give a Dopamine Receptor Antagonist (Prochlorperazine 10mg PO prechemo, then q4-6h PRN, OR Metoclopramide 10mg PO prechemo, then q4-6h PRN)

Continued Next Page

LU-CISP-GEM

CLINICAL MONITORING

- **Complete blood count** including differential, platelets and hemoglobin (CBC) and serum electrolytes [including Mg] before each cycle of treatment
- **Renal function tests** [serum creatinine & BUN] and **hepatic function** [serum Bilirubin] checked before each cycle of chemotherapy
- Check for **edema** at each visit
- **Hearing & Neurologic** toxicity ratings (Sensory)- each visit

HEARING

- 0 No change
- 1 Asymptomatic
- 2 Tinnitus
- 3 Correctable hearing loss
- 4 Deafness

SENSORY

- 0 No change
- 1 Mild paraesthesia: no deep tendon reflex
- 2 Mild/moderate sensory loss, moderate paraesthesia
- 3 Sensory loss interferes with function

Rated at each clinic visit

EDEMA

- 0 None
- 1 1+ or dependant evening only
- 2 2+ or dependant throughout the day
- 3 3+
- 4 4+, generalized anasarca

Rated if Edema noted on routine visits

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

DOSE MODIFICATION

Hematologic Toxicities

- 1. If ANC < $1.5 \times 10^9/L$, or if Platelets < $100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Renal failure (Recommended action)

- 1. If CrCl = 30-60mL/min or Serum Creatinine = 136-185µmol/L, reduce Cisplatin to **50%** dose
- 2. If CrCl < 30mL/min or Serum Creatinine > 185µmol/L, **Omit** Cisplatin dose

Gastrointestinal Toxicities

- 1. If Mucositis or Diarrhea ≥ Grade 3 in previous course, **REDUCE** to **50%** dose

NOTE

The recommended first-line chemotherapy regimen for stage IV Non-Small Cell Lung Cancer patients is either Cisplatin-Vinorelbine or Paclitaxel-Carboplatin (for patients who cannot tolerate Cisplatin). Other regimens have been explored for this disease, but without significant improvement in outcomes. Prescribers should be prepared to justify the use of this regimen in place of the standard regimens.

PATIENT VISIT

CHEMOTHERAPY VISIT:

Approx. 2 hours

27

LU-CISP-VINOR

Cisplatin-Vinorelbine

Chemotherapy

(Recurrent Metastatic Non-Small Cell
Lung Cancer)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

PREHYDRATION Day 1

- Encourage patient to drink 6-8 glasses of water prior to chemo each day
- May give Normal Saline 1000mL; Infuse over 1 hour

VINORELBINE 25mg/m² IV Days 1, 8, 15 & 22 (Round to nearest 1mg)

May reduce dose to 20mg/m² IV or omit Day 22 dose (if poorly tolerated)

- Slow push through sidearm of free flowing IV (Normal Saline 250mL);
Infuse over 6-10 minutes; infuse balance of IV bag
- If extravasation occurs during administration, discontinue immediately and
infuse the remaining dose through another IV site (into another vein)

CISPLATIN 80mg/m² IV Day 1

- Mix drug in 500mL Normal Saline; Infuse over 60 minutes
- May also give 200mL of 10% Mannitol solution (20G); infuse through
sidearm concurrent with Cisplatin (if diuresis needed)

POSTHYDRATION Day 1

- May give 1000mL Normal Saline (may add 10mEq/L Potassium Chloride and
8mmol/L Magnesium Sulphate); Infuse over 1 hour on Day 1

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

Cisplatin Day 1 - HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist IV prechemo (Ondansetron 8mg IV; OR
Granisetron 1mg IV; OR Dolasetron 100mg IV), **AND**
- Dexamethasone 20mg IV, **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if
given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron
given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for
1-2 days, if given pre-chemo, **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo
(Aprepitant 80 mg PO q 24 hours for 3 days) *When available in Canada*
- Oral hydration is strongly encouraged: poorly hydrated patients may need
more IV hydration (to prevent renal toxicity)

Vinorelbine Only Days - LOW RISK

- May give a Dopamine Receptor Antagonist (Prochlorperazine 10mg PO
prechemo, then q4-6h PRN; OR Metoclopramide 10mg PO prechemo, then
q4-6h PRN)

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LU-CISP-VINOR

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes [including Mg^{2+}] before each cycle of treatment
- Renal function tests [serum creatinine, electrolytes & BUN] and hepatic function [serum Bilirubin] checked before each cycle of chemotherapy
- Hearing & Neurologic toxicity ratings (Sensory)- each visit

HEARING

0. No change
1. Asymptomatic
2. Tinnitus
3. Correctable hearing loss
4. Deafness

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss; moderate paraesthesia
3. Sensory loss interferes with function

Rated at each clinic visit

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.5 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Renal failure (Recommended action)

1. If CrCl = 30-60mL/min or Serum Creatinine=136-185 μ mol/L, reduce Cisplatin to **50%** dose
2. If CrCl < 30 mL/min or Serum Creatinine $> 185\mu$ mol/L, **Omit** Cisplatin dose

Hepatic dysfunction

1. If AST = 60-180IU/L or Bili = 36-50 μ mol/L, **reduce** Vinorelbine to **50%** dose
2. If AST > 180 IU/L or Bili $> 50\mu$ mol/L, **reduce** Vinorelbine to **25%** dose

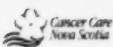
PATIENT VISIT

CHEMOTHERAPY VISITS At Cancer Centre:

Cisplatin Days = 4 to 6 hours
(depending on hydration)

Vinorelbine Days = 30 minutes

CT



LU-DOCETAX

Docetaxel Chemotherapy

(Non-Small Cell Lung Cancer- 2nd Line
Treatment for Platinum-Resistant
Tumours)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

PREMEDICATIONS:

DEXAMETHASONE 8mg PO, 3 doses before chemotherapy (evening before, morning of and 1 hour before chemotherapy), then 8mg PO BID for 3 doses after chemotherapy

DOCETAXEL 75 mg/m² IV Day 1 (Round to nearest 3mg)

- Mix in 250mL bag (5% Dextrose or Normal Saline) to a maximum concentration of 1.0-0.3mg/mL; Use non-PVC tubing; Infuse through main IV line over 1 hour

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

INTERMEDIATE RISK

Pre-Chemotherapy-

- Dopamine Receptor Antagonist PO (Prochlorperazine 10mg PO, or Metoclopramide 10mg PO)

Post-Chemotherapy-

- Dopamine Receptor Antagonist PRN ((Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10mg PO q4h PRN)

DEXAMETHASONE Alternate Pre- & Postmedication Regimens:

- May give 20mg PO 12hr & 6hr before chemotherapy, then 8mg PO bid for 4 days after chemotherapy
- May give 8mg PO at 13hr, 7hr & 1hr before chemotherapy, then 8mg PO bid for 3 days after chemotherapy

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Hepatic dysfunction

1. If AST or ALT > 60 IU/L (> 1.5X ULN) or if Alk Phos > 300 IU/L (> 2.5X ULN), reduce Docetaxel to **75% dose**
2. If AST or ALT > 200 IU/L (> 5X ULN) or if Alk Phos > 600 IU/L (> 5X ULN), **HOLD** Docetaxel dose and contact physician

ALTERNATE ADJUSTMENT

3. If LFTs > 1.5x ULN or Bilirubin > ULN (> 26 µmol/L) during treatment, **HOLD** Docetaxel dose for 3 weeks and re-test
ULN = upper limit of normal for lab value
(Recommended action)

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

Continued Next Page...

LU-DOCETAX

CLINICAL MONITORING

- **Complete blood count** including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- **Baseline liver function tests** (if liver failure suspected) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]
- Watch for symptoms of **fever or infection**
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Skin assessment** at each visit, including nails and infusion veins
- Monitor **fluid retention** at each visit

SKIN TOXICITY

0. None
1. Hyperpigmentation
2. Atrophy
3. Subcutaneous fibrosis
4. Desquamation, ulceration, or necrosis

NAIL CHANGES

0. Normal
1. Discolouration or ridging (Vailonychia) or pitting
2. Partial or complete loss of nail(s) or pain in nailbeds
3. -
4. -

FLUID RETENTION

0. None
1. Mild peripheral edema
2. Pleural edema, outpatient management
3. Pleural edema, inpatient management
4. Intubation required

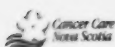
Rated at each clinic visit

NOTE

This chemotherapy is generally used as second-line treatment for patients with good performance status who are motivated to try a second course of chemotherapy.

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT
Approximately 2 hours



LU-TOPO

Topotecan Chemotherapy

(Small Cell Lung Cancer- Palliative Treatment)

BASIC LEVEL REGIMEN-
Community Hospital with Oncology Nurses

TOPOTECAN 1.25mg/m² IV Days 1 to 5 (Round to nearest 0.1mg)

- Mix in 50-100mL minibag (5% Dextrose or Normal Saline); Infuse over 30 minutes
- Final concentration should be 10mcg-500mcg/mL

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: INTERMEDIATE RISK

Pre-Chemotherapy (on Days 1 to 5)-

- Dexamethasone 8 mg PO, **AND/OR**
- Dopamine Receptor Antagonist PO (Metoclopramide 10mg PO, **OR** Prochlorperazine 10mg PO)

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses; **AND/OR**
- Dopamine Receptor Antagonist PO (Metoclopramide 10mg PO q4-6h PRN, **OR** Prochlorperazine 10mg PO q4-6h PRN)

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Baseline renal function tests (if failure suspected) [serum creatinine, electrolytes & BUN]

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

GUIDELINE

See the CCNS website
www.cancercare.ns.ca for the guideline on Topotecan for ovarian cancer

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Renal failure (Suggested action)

1. If CrCl = 20-40 mL/min, **reduce** to **50%** dose of Topotecan
2. If CrCl < 20 mL/min, **OMIT** dose of Topotecan

PATIENT VISIT

CHEMOTHERAPY VISIT: Approx. 20 minutes

NOTE

The recommended first-line chemotherapy regimen for stage IV Non-Small Cell Lung Cancer patients is either Cisplatin-Vinorelbine or Paclitaxel-Carboplatin (for patients who cannot tolerate Cisplatin). Other regimens have been explored for this disease, but without significant improvement in outcomes.

[Rev 05/02]

LU-VINOR

Vinorelbine Chemotherapy

(Non-Small Cell Lung Cancer)

**INTERMEDIATE LEVEL
REGIMEN**- Regional Hospital with
Dedicated Cancer Treatment Unit

VINORELBINE 30mg/m² IV Day 1 & Day 8 (or Day 15) (Round to nearest 1mg)

May reduce dose to 25mg/m² IV (for frail, elderly or heavily-pretreated patients)

- Slow push through sidearm of free flowing IV (Normal Saline 250mL); Infuse over 6-10 minutes; infuse balance of IV bag
- If extravasation occurs during administration, discontinue immediately and infuse the remaining dose through another IV site (into another vein)

REPEAT EVERY 21 DAYS - May give Days 1, 8 & 15 every 28 days,
or weekly until blood counts below threshold

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- May give Dopamine Receptor Antagonist PO before chemotherapy (Prochlorperazine 10mg PO or Metoclopramide 10-20mg PO)
- After chemotherapy, use Prochlorperazine 10 mg PO q4-6h PRN, or Metoclopramide 10 mg PO q4h PRN

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, notify physician and **HOLD** dose (Until ANC ≥ 1.5 x 10⁹/L)

Hepatic dysfunction

1. If AST = 60-180IU/L or Bili = 36-50µmol/L, **reduce** Vinorelbine to **50%** dose
2. If AST > 180IU/L or Bili > 50µmol/L, **reduce** Vinorelbine to **25%** dose

PHYSICIAN'S STANDING ORDERS AVAILABLE FOR THIS REGIMEN

NOTE

The usual chemotherapy regimen for stage IV Non-Small Cell Lung Cancer patients is Cisplatin-Vinorelbine. This regimen may be chosen for patients who cannot tolerate Cisplatin. Outcomes are inferior to Cisplatin-Vinorelbine, so another regimen might be considered.

CLINICAL MONITORING

- **Complete blood count including differential, platelets and hemoglobin (CBC) and serum uric acid levels** before each cycle of treatment
- **Liver function tests** [GGT, ALT, AST & Bilirubin levels] at baseline and on Day 1 of each cycle of treatment
- **Neurologic toxicity ratings** (Sensory, Constipation) at each visit
- Watch for symptoms of **fever or infection**

CONSTIPATION

0. No change
2. Mild
3. Moderate
4. Severe
4. Ileus >96 hours

SENSORY

0. No change
 1. Mild paraesthesia; no deep tendon reflex
 2. Mild/moderate sensory loss; moderate paraesthesia
 3. Sensory loss interferes with function
- Rated at each clinic visit**

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:
Approx. 30 minutes

[Rev 07/02]

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NOTE: Regimen names in italics are
not in this pocketbook version- See
full version for regimen monograph

**Doxorubicin-Bleomycin-
Vinblastine-Dacarbazine
(ABVD) Chemotherapy**

(Hodgkin's Lymphoma- Curative Intent)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

DOXORUBICIN 25mg/m² IV Days 1 & 15 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV; Give over at least 3-5 minutes

VINBLASTINE 6mg/m² IV Days 1 & 15 (Round to nearest 0.1mg)

- Quick push through sidearm of free flowing IV; Inject over 1 minute

BLEOMYCIN 10mg/m² IV Days 1 & 15 (Round to nearest 1mg)

- Mix in 50mL minibag (Normal Saline); Infuse over 15 minutes

DACARBAZINE 375mg/m² IV Days 1 & 15 (Round to nearest 10mg)

- Mix in 500mL bag (Normal Saline); Infuse through main IV line, with an additional 500mL Normal Saline run at same time by piggyback, to reduce vein irritation
- Infuse over 60 minutes; If vein irritation, infuse more slowly
- PROTECT FROM LIGHT

REPEAT EVERY 28 DAYS For a Usual Total of 6 to 8 Cycles

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy (Days 1 & 15)-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, OR Granisetron 2mg PO or 1mg IV, OR Dolasetron 100mg PO or 100mg IV), **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum uric acid levels before each cycle of treatment
- Clinical pulmonary exam at each visit, including auscultation, pulmonary toxicity ratings (Cough, SOB toxicity ratings)
- Baseline renal function tests (if failure suspected) [serum creatinine, electrolytes & BUN] & liver function tests (especially if poor Performance Status) (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated)
- Clinical exam for symptoms of **Congestive Heart Failure**
- Periodic cardiac tests for all patients with cardiac risk factors or patients at or above the threshold dose levels
- Neurologic toxicity ratings (Sensory toxicity ratings) at each visit

Continued Next Page...

LY-ABVD

CLINICAL MONITORING

COUGH

0. None
1. Mild
2. Moderate
3. Severe

SHORT OF BREATH

0. No change
1. Mild SOB
2. Dyspnea on exertion
3. Dyspnea at normal level of activity
4. Dyspnea at rest

Rated at each clinic visit, if Bleomycin dosage needs adjustment

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss; moderate paraesthesia
3. Sensory loss interferes with function

Rated at each clinic visit

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.0 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, notify physician and give **50%** dose of Doxorubicin & Vinblastine
2. If ANC $< 0.8 \times 10^9/L$, or if Platelets $< 75 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Renal failure

1. If CrCl = 12-60mL/min, reduce Bleomycin to **75%** dose
2. If CrCl < 12 mL/min, reduce Bleomycin to **50%** dose
(Recommended action)
3. If Serum Creatinine $> 265\mu\text{mol/L}$, reduce Doxorubicin to **50%** dose (Suggested action)
- Hepatic dysfunction
1. If Bili = 26-51 $\mu\text{mol/L}$ or AST = 60-180IU/L, **reduce** Doxorubicin & Vinblastine to **50%** dose
2. If Bili = 52-85 $\mu\text{mol/L}$ or AST > 180 IU/L, **reduce** Doxorubicin & Vinblastine to **25%** dose
3. If Bili $> 85\mu\text{mol/L}$, **Omit** Doxorubicin & Vinblastine doses (Recommended action)
4. Consider dose reduction of Dacarbazine if renal function is reduced (eg. reduced creatinine clearance/serum creatinine)(Suggested action)

Renal failure (Recommended actions)

1. If CrCl = 12-48mL/min, **reduce** Bleomycin to **75%** dose
2. If CrCl < 12 mL/min, **reduce** Bleomycin to **50%** dose

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:
Approx. 2 hours

LY-MINI-BEAM

Carmustine-Etoposide- Cytarabine-Melphalan (Mini- BEAM Modified)

SPECIALIZED LEVEL REGIMEN-
Capital Health Cancer Care
Program ONLY

*(Preparatory Regimen before High Dose Treatment with Bone Marrow/Stem
Cell Rescue- Curative Intent)*

CARMUSTINE 60mg/m² IV Day 1 (Round to nearest 3mg)

- Mix in 250mL fluid in polyolefin bag (5% Dextrose)- Use non-PVC tubing
- Protect from light
- Infuse over 60 minutes or longer (slower infusion, if poorly tolerated)
- Hydration with Normal Saline infused at 50mL/hr, starting 60 minutes before first dose

ETOPOSIDE 75mg/m² IV Days 1 to 4 (Round to nearest 10mg)

- Premixed in 500mL bags of Normal Saline; connect piggyback to IV line;
Infuse over 60 minutes

CYTARABINE 100mg/m² IV q12h Days 1 to 4-Total of 8 doses (Round to nearest 10mg)

- May be mixed in 250mL bag (Normal Saline); Infuse over 30 minutes
- For ambulatory care, may dispense a prefilled bag for home infusion, if home nursing is available (dispense daily interim doses, daytime doses given in treatment centre)

MELPHALAN 30mg/m² IV Day 5 (Round to nearest 5mg; Maximum dose = 50mg)

- Mix in 100mL bag (Normal Saline); Infuse over 15 minutes
- Complete infusion within 60 minutes of dose preparation

REPEAT EVERY 21 to 28 DAYS

Repeat treatments when adequate marrow recovery

SUPPORTIVE CARE

ANTIEMETIC REGIMENS: Day 1 - HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO prechemo and qHS on Day 1- may substitute Ondansetron 8mg IV, OR Granisetron 2mg PO or 1mg IV prechemo, OR Dolasetron 100mg PO or 100mg IV prechemo), AND
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)
- May add Lorazepam 2mg SL/PO on days 1 to 4, before chemo

Days 2 to 5 - INTERMEDIATE RISK

Pre-Chemotherapy-

- Dexamethasone 4-8 mg PO before each Etoposide dose, and
- Dopamine Receptor Antagonist PO (Metoclopramide 10-20mg PO/IV, OR Prochlorperazine 10mg PO/IV) before each dose of Etoposide or Melphalan

Post-Chemotherapy-

- Dopamine Receptor Antagonist PO (Metoclopramide 10mg PO q4h PRN; OR Prochlorperazine 10mg PO q4-6h PRN)

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

LY-MINI-BEAM

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC), serum electrolytes (including Ca^{2+} , Mg^{2+} & PO_4) and serum uric acid levels before each cycle of treatment
- Baseline renal function tests (if failure suspected) [serum creatinine, electrolytes & BUN] & liver function tests (especially if poor Performance Status) (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated)
- Clinical pulmonary exam at each visit, including auscultation, pulmonary toxicity ratings (Cough, SOB)
- Baseline renal function tests (if failure suspected) [serum creatinine, electrolytes & BUN]
- Clinical assessment of stomatitis, oral examination upon patient complaint of a sore mouth
- Baseline blood pressure at each Etoposide treatment, monitor for hypotension
- Watch for symptoms of fever or infection

COUGH

- 0 None
- 1 Mild
- 2 Moderate
- 3 Severe

SHORT OF BREATH

- 0 No change
- 1 Mild SOB
- 2 Dyspnea on exertion
- 3 Dyspnea at normal level of activity
- 4 Dyspnea at rest

Rated at each clinic visit

Cumulative Carmustine Lifetime Dose Limit 1400mg/m²

DOSE MODIFICATION

Hematologic Toxicities

- 1 If ANC $< 1.0 \times 10^9/\text{L}$, or if Platelets $< 100 \times 10^9/\text{L}$, notify physician and **HOLD** dose for 1 week

Renal failure (Suggested action)

- 1 If CrCl $< 60\text{mL/min}$, reduce Carmustine dose by **25-50%**
- 2 If CrCl = $12-48\text{mL/min}$ or Serum Creatinine $> 130\mu\text{mol/L}$, reduce Melphalan & Etoposide to **75%** dose
- 3 If CrCl $< 12\text{mL/min}$, reduce Melphalan to **50%** dose and Carmustine to **25-50%** dose

Hepatic dysfunction

- 1 If Bili= $26-51\mu\text{mol/L}$ or AST= $60-180\text{IU/L}$, reduce Etoposide to **50%** dose
- 2 If Bili= $52-85\mu\text{mol/L}$, reduce Etoposide to **25%** dose
- 3 If Bili $> 85\mu\text{mol/L}$ or AST $> 180\text{IU/L}$, **Omit** Etoposide dose (Suggested action)

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

NOTE

Mini-BEAM modified for ambulatory treatment at Cancer Centre and in the home

LY-CHLORAM

Chlorambucil* PO Chemotherapy

Take-Home Prescription-
Unrestricted

(Non-Hodgkin's Lymphoma (Low Grade)- Palliative Intent)

CHLORAMBUCIL 40 mg/m² PO Day 1

OR 8mg/m² PO daily for 14 days OR 4-10mg PO daily for 21 days

OR 3 to 6mg/m² PO daily until WBC < 10 x 10⁹/L, then 1 to 2mg/m² PO daily

(Outpatient prescription in multiples of 2mg tablets) (dosage may vary)

May also add:

PREDNISONE 50 mg PO daily for 5 to 10 days (dosage may vary)

(Outpatient prescription in multiples of 5mg and 50mg tablets)

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic before chemotherapy
- After chemotherapy, use Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q3-4h PRN

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.0 x 10⁹/L, or if Platelets < 100 x 10⁹/L, **HOLD** dose for 1 week

Hepatic dysfunction (Suggested action)

1. Consider dose reduction if LFTs elevated (eg. Bilirubin or AST)

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum uric acid levels before each cycle of treatment
- Clinical pulmonary exam at each visit, incl auscultation, pulmonary toxicity ratings

SHORT OF BREATH

- 0 No change
- 1 Mild SOB
- 2 Dyspnea on exertion
- 3 Dyspnea at normal level of activity
- 4 Dyspnea at rest

Rated at periodic clinic visits, at each visit after 6 months' treatment, or upon patient complaint

LY

LY-CHL-VPP

Chlorambucil-Vinblastine- Procarbazine-Prednisone (CHL-VPP) Chemotherapy

(Hodgkin's Lymphoma)

INTERMEDIATE LEVEL REGIMEN

(Vinblastine)- Regional Hospital
with Dedicated Cancer Treatment
Unit

Take-Home Prescription

(Chlorambucil, Procarbazine,
Prednisone)- Unrestricted

VINBLASTINE 6mg/m² IV Day 1 & Day 8 (Round to nearest 0.1mg)

• Quick push through sidearm of free flowing IV; Inject over 1 minute

CHLORAMBUCIL 6mg/m² PO for 14 days

(Outpatient prescription in multiples of 2mg tablets)

PROCARBAZINE 100mg/m² PO for 14 days

(Outpatient prescription in multiples of 50mg capsules)

PREDNISONE 40mg PO for 14 days

(Outpatient prescription in multiples of 5mg & 50mg tablets)

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic before chemotherapy
- After chemotherapy use
Prochlorperazine 10mg PO q4-6h
PRN or Metoclopramide 10mg PO
q3-4h PRN

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.0 x 10⁹/L, or if Platelets < 100 x 10⁹/L, notify physician and give 50% dose of Chlorambucil, and Procarbazine
2. If ANC < 0.8 x 10⁹/L, or if Platelets < 75 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Renal failure

1. Consider dose reduction of Procarbazine if renal function is reduced (eg. reduced creatinine clearance/serum creatinine)
(Suggested action)

Hepatic dysfunction

1. If Bili = 25-50µmol/L or AST = 60-180IU/L, reduce Vinblastine to **50%** dose
2. If Bili > 50µmol or AST > 180IU/L, reduce Vinblastine to **25%** dose
(Recommended actions)
3. Consider dose reduction of Chlorambucil if LFTs elevated (eg. Bilirubin or AST)

LY-CHL-VPP

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum uric acid levels before each cycle of treatment
- Serum glucose levels (monitor routinely for diabetic patients)
- Clinical pulmonary exam at each visit, including auscultation, pulmonary toxicity ratings (SOB)
- Neurologic toxicity ratings (Sensory) at each visit

SENSORY

- 0 No change
- 1 Mild paraesthesia; no deep tendon reflex
- 2 Mild/mod sensory loss; mod paraesthesia
- 3 Sensory loss interferes with function

Rated At Each Clinic Visit

SHORT OF BREATH

- 0 No change
- 1 Abnormal PFT's
- 2 Dyspnea on exertion
- 3 Dyspnea at normal level of activity
- 4 Dyspnea at rest

COUGH

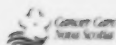
- 0 None
- 1 Mild
- 2 Moderate
- 3 Severe

Rated at each clinic visit every 2-3 months

PATIENT VISIT

CHEMOTHERAPY VISIT:

Approximately 20-30 minutes



LY-CHOP

Cyclophosphamide-Doxorubicin-Vincristine- Prednisone (CHOP) Chemotherapy

(Non-Hodgkin's Lymphoma)

INTERMEDIATE LEVEL REGIMEN
Regional Hospital with Dedicated Cancer Treatment Unit

DOXORUBICIN 50mg/m² IV Day 1 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV, Give over at least 3-5 minutes

VINCRIStINE 1.4mg/m² IV Day 1

- Push through sidearm of free flowing IV, Inject over at least 1 minute

CYCLOPHOSPHAMIDE 750mg/m² IV Day 1 (Round to nearest 10mg)

- Mix in 250mL bag (Normal Saline); Infuse over 30 minutes

PREDNISONE 150mg PO for 5 days

(Outpatient prescription in multiples of 50mg tablets)

REPEAT EVERY 21 DAYS

For a Usual Total of 6 to 8 Cycles

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)
- Oral hydration is strongly encouraged, poorly hydrated patients may need more IV hydration

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.0 x 10⁹/L, or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week (Until ANC ≥ 1.0 x 10⁹/L)

Renal failure

1. If Serum Creatinine >265µmol/L, reduce Doxorubicin to **50%** dose
2. If CrCl < 12mL/min, **OMIT** Cyclophosphamide dose (Suggested action)

Hepatic dysfunction

1. If Bili=26-51µmol/L or AST =60-180IU/L, reduce Doxorubicin and Vincristine to **50%** dose
2. If Bili= 52-85µmol/L or AST>180IU/L, reduce Cyclophosphamide to **75%** dose, & Doxorubicin and Vincristine to **25%** dose
3. If Bili > 85µmol/L, **OMIT ALL** drugs (Suggested action)

Continued Next Page...

LY-CHOP

CLINICAL MONITORING

- **Complete blood count** including differential, platelets and hemoglobin (CBC) and **serum electrolytes** before each cycle of treatment
- Baseline **renal function tests** (if failure suspected) [serum creatinine, electrolytes & BUN] & **liver function tests** (especially if poor Performance Status) (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated)
- **Serum glucose** levels (monitor routinely for diabetic patients)
- Periodic **urinalysis (RBCs)** and in response to patient complaint
- **Neurologic toxicity** ratings at each visit
- Clinical exam for symptoms of **Congestive Heart Failure**
- Periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels

CONSTIPATION

0. No change
1. Mild
2. Moderate
3. Severe
4. Ileus >96 hours

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss, moderate paraesthesia
3. Sensory loss interferes with function

Rated at each clinic visit

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:
Approx. Approx. 2-3 hours

LY

LY-CVP*IV

Cyclophosphamide IV- Vincristine-Prednisone (CVP*IV) Chemotherapy

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

(Non-Hodgkin's Lymphoma (Low Grade)- Palliative Intent)

VINCRISTINE 2 mg/m² IV Day 1 (Round to nearest 0.1mg)

• Push through sidearm of free flowing IV; Inject over at least 1 minute

CYCLOPHOSPHAMIDE 750 mg/m² IV Day 1 (Round to nearest 10mg)

• Mix in 250mL bag (Normal Saline); Infuse over 20-30 minutes

PREDNISONE 100 mg PO for 5 days

(Outpatient prescription in multiples of 50mg tablets)

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

INTERMEDIATE RISK

Pre-Chemotherapy-

- Dopamine Receptor Antagonist PO (e.g. Metoclopramide 10-20mg PO, or Prochlorperazine 10mg PO)

Post-Chemotherapy-

- Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10mg PO q3-4h PRN

OTHER SUPPORTIVE CARE

- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration (to prevent renal toxicity)

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes before each cycle of treatment
- Baseline renal function tests (if failure suspected) [serum creatinine, electrolytes & BUN]
- Serum glucose levels (monitor routinely for diabetic patients)
- Periodic urinalysis (RBCs); Cystitis toxicity ratings in response to patient complaint
- Neurologic toxicity ratings (Sensory, Constipation) at each visit

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss; moderate paraesthesia
3. Sensory loss interferes with function

CONSTIPATION

0. No change
1. Mild
2. Moderate
3. Severe
4. Ileus >96 hours

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.0 x 10⁹/L, or if Platelets < 100 x 10⁹/L, **HOLD** dose for 1 week

Hepatic dysfunction (Suggested action)

1. If Bili = 25-50µmol/L or AST = 60-180IU/L, reduce Vincristine to **50%** dose
2. If Bili = 51-85µmol/L or AST > 180IU/L, reduce Vincristine to **25%** dose & Cyclophosphamide to **75%** dose
3. If Bili > 85µmol/L, **Omit** Cyclophosphamide & Vincristine

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

PATIENT VISIT

CHEMOTHERAPY VISIT:

Approximately 30-45 minutes

[Rev 11/01]

LY-CVP*PO

Cyclophosphamide PO- Vincristine-Prednisone (CVP*PO) Chemotherapy

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

(Non-Hodgkin's Lymphoma (Low Grade)- Palliative Intent)

VINCRIStINE 1.2 mg/m² IV Day 1

(Round to nearest 0.1mg- To a maximum dose of 2mg)

- Push through sidearm of free flowing IV, Inject over at least 1 minute

CYCLOPHOSPHAMIDE 300 to 450 mg PO for 5 days

(Outpatient prescription in multiples of 25mg & 50mg tablets)

PREDNISONE 75 to 150 mg PO for 5 days

(dose may be tapered down after 5 days) (Outpatient prescription in multiples of 50mg tablets)

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic before chemotherapy
- After chemotherapy, use Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10mg PO q3-4h

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.0 x 10⁹/L, or if Platelets < 100 x 10⁹/L, **HOLD** dose for 1 week

Hepatic dysfunction (Suggested action)

1. If Bili = 25-50µmol/L or AST = 60-180IU/L, reduce Vincristine to **50%** dose
2. If Bili = 51-85µmol/L or AST > 180IU/L, reduce Vincristine to **25%** dose & Cyclophosphamide to **75%** dose
3. If Bili > 85µmol/L, **Omit** Cyclophosphamide & Vincristine

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

PATIENT VISIT

CHEMOTHERAPY VISIT:

Approximately 20-30 minutes

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes before each cycle of treatment
- Baseline renal function tests (if failure suspected) [serum creatinine, electrolytes & BUN]
- Serum glucose levels (monitor routinely for diabetic patients)
- Periodic urinalysis (RBCs), Cystitis toxicity ratings in response to patient complaint
- Neurologic toxicity ratings (Sensory, Constipation) at each visit

SENSORY

0. No change
1. Mild paraesthesia, no deep tendon reflex
2. Mild/moderate sensory loss, moderate paraesthesia
3. Sensory loss interferes with function

CONSTIPATION

0. No change
1. Mild
2. Moderate
3. Severe
4. Ileus >96 hours

LY-CYCLO*PO

Cyclophosphamide*PO Chemotherapy

Take-Home Prescription-
Unrestricted

(Non-Hodgkin's Lymphoma (Low Grade)- Palliative Intent)

CYCLOPHOSPHAMIDE 50-200mg PO daily for 14 days
(Outpatient prescription in multiples of 25mg & 50mg tablets)

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic before chemotherapy
- After chemotherapy, use Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10mg PO q3-4h PRN

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC $< 1.0 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, **HOLD** dose for 1 week

Hepatic dysfunction (Suggested action)

1. If Bilirubin = 51-85 $\mu\text{mol/L}$ or AST $> 180 \text{ IU/L}$, reduce Cyclophosphamide to **75%** dose
2. If Bilirubin $> 85 \mu\text{mol/L}$, **Omit** Cyclophosphamide

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes before each cycle of treatment
- Baseline renal function tests (if failure suspected) [serum creatinine, electrolytes & BUN]
- Periodic urinalysis (RBCs) and in response to patient complaint

LY

LY-DHAP

ADVANCED LEVEL REGIMEN-
Provincial Cancer Centre

Cisplatin-Cytarabine (High Dose)-Dexamethasone (DHAP) Chemotherapy

(Non-Hodgkin's Lymphoma (Salvage Therapy- Advanced Stage)- Palliative Intent)

PREHYDRATION

- 2000mL Normal Saline with 20mEq/L Potassium Chloride, 4mmol/L Magnesium Sulphate and 20G/L Mannitol; Infuse at 250mL/hr for 6 hours **BEFORE** Cisplatin

CISPLATIN 100mg/m² CIV over 24 hours Day 1 (Round to nearest 1mg)

- Hydration: Continue same solution at 125mL/hr **DURING** Cisplatin infusion; Infuse through a separate line from the Cisplatin (solutions not compatible)
- Mix equal thirds of Cisplatin in 3 x 1000mL Normal Saline; Infuse each bag over 8 hours in sequence (total dose diluted in 3000mL)

POSTHYDRATION

- 1000mL Normal Saline with 20mEq/L Potassium Chloride, 4mmol/L Magnesium Sulphate and 20G/L Mannitol; Infuse at 200mL/hr for 6 hours **AFTER** Cisplatin

CYTARABINE 2000mg/m² CIV over 3 hours, repeat 12 hours later Day 2

- Start immediately after Cisplatin (Total dose = 4000mg/m², as 2 doses of 2000mg/m²)
- Mix in 250mL Normal Saline; Infuse over 3 hours each dose

DEXAMETHASONE 40mg PO or IV Days 1 to 4

(Outpatient prescription in multiples of 4mg tablets)

- Mix dose in 50mL Normal Saline; Infuse over 15 minutes, if dose given IV

REPEAT EVERY 21-28 DAYS

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC), serum electrolyte levels and serum uric acid levels before each cycle of treatment
- Baseline and routine renal function tests [serum creatinine, electrolytes & BUN] before each cycle - especially if there are other concurrent nephrotoxic drugs
- **Hearing & Neurologic** toxicity ratings (Sensory)- each visit
- Serum glucose levels (for diabetic patients on multiple day treatments)
- Baseline and periodic urine output and urinalysis tests with high doses
- Clinical exam for proximal muscle myopathy

HEARING

0. No change
1. Asymptomatic
2. Tinnitus
3. Correctable hearing loss
4. Deafness

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss; moderate paraesthesia
3. Sensory loss interferes with function

Rated At Each Clinic Visit

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

Continued Next Page...

LY-DHAP

CLINICAL MONITORING

High Dose Cytarabine:

- Close neurological and systemic monitoring of all organs (before each dose) while drug is administered in hospital
- Clinical pulmonary exam at each visit, including auscultation, pulmonary toxicity ratings (especially within the first month after treatment)
- Cerebellar and sensory toxicity ratings each visit, for the first few weeks after treatment

CEREBELLAR

0. None
1. Slight incoordination, dysdiadochokinesis
2. Intention tremor, dysmetria, slurred speech, nystagmus
3. Locomotor ataxia
4. Cerebellar necrosis

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: Days 1 & 2 - HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO/IV (i.e. Ondansetron 8-16mg PO or 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), and
- Dexamethasone 20mg IV
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
When available in Canada

Post-Chemotherapy-

- Dexamethasone 8 mg PO twice daily for 2 to 3 days, and
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *When available in Canada*
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration (to prevent renal toxicity)

OTHER SUPPORTIVE CARE

- May give Allopurinol 300mg PO qd for 5 days, starting on Day 1
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration (to prevent renal toxicity)

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < $1.0 \times 10^9/L$, or if Platelets < $100 \times 10^9/L$, **HOLD** dose for 1 week

Renal failure (Recommended action)

1. If CrCl = 30-60mL/min or Serum Creatinine = 136-185µmol/L, **reduce** Cisplatin to **50%** dose
2. If CrCl < 30mL/min or Serum Creatinine > 185µmol/L, **OMIT** Cisplatin dose

[Rev. 10/02]

LY-FLUDAR

Fludarabine Chemotherapy

(Low Grade Lymphoma- Palliative Intent)

BASIC LEVEL REGIMEN-

Community Hospital with Oncology Nurses

FLUDARABINE 25 mg/m² IV Days 1 to 5 (Round to nearest 2.5mg)

• Mix in 50mL minibag (Normal Saline); Infuse over 15-30 minutes

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- Prochlorperazine 10mg PO (&/or PR) q4-6h PRN *OR*
- Dexamethasone 4-8mg PO q6-12h PRN for 1 to 5 days *OR BOTH*

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.0 x 10⁹/L, or if Platelets < 100 x 10⁹/L, **HOLD** dose for 1 week

PHYSICIAN'S STANDING ORDERS AVAILABLE FOR THIS REGIMEN

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum uric acid levels before each cycle of treatment
- Periodic clinical pulmonary exam, including auscultation, pulmonary toxicity ratings
- Watch for symptoms of fever or infection

SHORT OF BREATH

0. No change
1. Mild Shortness of Breath
2. Dyspnea on exertion
3. Dyspnea at normal level of activity
4. Dyspnea at rest

Rated at periodic clinic visits and in response to patient complaints

NOTE

ALWAYS use irradiated blood products after Fludarabine given

PATIENT VISIT

CHEMOTHERAPY VISIT:

Approximately 30-45 minutes

LY

LY-MC*IT

**Methotrexate-Cytarabine
Intrathecal Chemotherapy**

(CNS Lymphoma, ALL)

ADVANCED LEVEL REGIMEN-
Provincial Cancer Centre

METHOTREXATE 12mg/m² INTRATHECAL

Once or twice weekly (by lumbar puncture or via ommaya reservoir)

(Dose may vary at discretion of prescribing hematologist)

(Administer concurrently with other Lymphoma Treatment)

AND / OR / ALTERNATING WITH:

CYTARABINE 70mg/m² INTRATHECAL

Once or twice weekly (by lumbar puncture or via ommaya reservoir)

(Dose may vary at discretion of prescribing hematologist)

- To be given as Intrathecal injection; use unpreserved solution or mix in unpreserved diluent using strict aseptic technique; dilute to a total volume of 3mL

- Patient instructed to lie flat for 30-60 minutes after intrathecal injection

- Do not give Methotrexate oral tablets during weeks on intrathecal injections

REPEAT ONCE OR TWICE WEEKLY

**INTRATHECAL AND INTRAVENOUS CHEMOTHERAPY MUST
NOT BE AT THE PATIENT'S BEDSIDE AT THE SAME TIME
(except continuous infusions)**

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic prophylaxis recommended

OTHER SUPPORTIVE CARE

- Cotrimoxazole DS (800/160) PO BID for 1-3 days after each injection

DOSE MODIFICATION

Hematologic Toxicities

1. If Platelets < 50 x 10⁹/L, **HOLD** dose (unless platelet transfusion is administered)
2. If INR > 1.5, and if PTT > 40, **HOLD** dose

NOTE

- This regimen should only be given by Hematologists trained in the administration of intrathecal chemotherapy.
- Schedule of IT dose(s) may be modified according to physician availability. Initiation of IT drug(s) should be deferred until stabilization of any coagulopathy and reduction of circulating blast count.

CLINICAL MONITORING

- Schedule of IT doses may be modified according to physician availability. Initialization of IT chemotherapy should be deferred until stabilization of any coagulopathy and reduction of circulating platelet count
- Methotrexate IT doses are flat doses and are NOT adjusted for body surface area

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

PATIENT VISIT

CHEMOTHERAPY VISIT:
Approximately 90 minutes

LY-MOPP

Mechlorethamine-Vincristine- Procarbazine-Prednisone (MOPP) Chemotherapy

(Hodgkin's Lymphoma)

ADVANCED LEVEL REGIMEN-

Provincial Cancer Centre

INTERMEDIATE LEVEL REGIMEN-

Regional Hospital with
Hematologist Supervision

MECHLORETHAMINE 6mg/m² IV day 1 & day 8

(Round to nearest 0.1mg)

- Slow push through sidearm of free flowing IV (5% Dextrose); Infuse at a rate no greater than 1mg/1mL per minute

VINCRIStINE 1.4mg/m² IV day 1 & day 8 (Round to nearest 0.1mg)

- Push through sidearm of free flowing IV; Inject over at least 1 minute

PROCARBAZINE 100mg/m² PO for 14 days

(Outpatient prescription in multiples of 50mg capsules)

PREDNISONE 50mg/m² PO for 14 days

(Outpatient prescription in multiples of 5mg & 50mg tablets)

REPEAT EVERY 28 DAYS FOR A USUAL TOTAL OF 6 CYCLES

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV)

Post-Chemotherapy-

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
- No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
- Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.0 x 10⁹/L, or if Platelets < 100 x 10⁹/L, give **50%** dose of Mechlorethamine and Procarbazine
2. If ANC < 0.8 x 10⁹/L, or if Platelets < 75 x 10⁹/L, **HOLD** dose for 1 week

Renal failure (Suggested action)

1. If CrCl = 12-48mL/min, **reduce** Mechlorethamine to **75%** dose
2. If CrCl < 12mL/min, **reduce** Mechlorethamine to **50%** dose
3. Consider dose reduction of Procarbazine if renal function is reduced (eg. reduced creatinine clearance/serum creatinine)

Hepatic dysfunction (Suggested action)

1. If Bili = 25-50µmol/L or AST = 60-180IU/L, **reduce** Vincristine to **50%** dose
2. If Bili > 50µmol/L or AST > 180IU/L, **reduce** Vincristine to **25%** dose

LY

LY-MOPP

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Serum glucose levels (monitor routinely for diabetic patients)
- Periodic clinical pulmonary exam, including auscultation, pulmonary toxicity ratings (SOB, Cough)
- Neurologic toxicity ratings at each visit

SHORT OF BREATH

- 0 No change
- 1 Abnormal PFT's
- 2 Dyspnea on exertion
- 3 Dyspnea at normal level of activity
- 4 Dyspnea at rest

COUGH

- 0 None
- 1 Mild
- 2 Moderate
- 3 Severe

CONSTIPATION

- 0 No change
- 1 Mild
- 2 Moderate
- 3 Severe
- 4 Ileus >96 hours

SENSORY

- 0 No change
- 1 Mild paraesthesia; no deep tendon reflex
- 2 Mild/moderate sensory loss; moderate paraesthesia
- 3 Sensory loss interferes with function

Rated at each clinic visit

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT

Approximately 1 hour

LY-RITUX

Rituximab Monotherapy

(Treatment of Relapsed or Refractory
Low-Grade or Follicular B-cell Non-
Hodgkin's Lymphoma which is CD-20
Positive)

**ADVANCED LEVEL REGIMEN (First
Cycle)-** Provincial Cancer Centre

INTERMEDIATE LEVEL REGIMEN
(Subsequent cycles- if no reaction)-
Regional Hospital with Dedicated
Cancer Treatment Unit

RITUXIUMAB 375mg/m² IV Days 1, 8, 15 & 22 Only

- Infuse IV at 50mg/hr, then increase by increments of 50mg/hr every 30 minutes, as tolerated, to a final rate of 400mg/hr for the first dose
- Subsequent infusions may be initiated at 100mg/hr and increased by increments of 100mg/hr every 30 minutes to the maximum rate of 400mg/hr, as tolerated by the patient
- Observe for 30-60 minutes after infusion
- Infusion-related symptoms may be managed by slowing or interrupting the infusion, and with the use of supportive care (including IV saline, acetaminophen, diphenhydramine, or bronchodilators, as needed)
- Mix in Normal Saline to designated volume for dose- Table of volumes and infusion rates for 2mg/mL, may dilute to final concentration of 1-4mg/mL
- **DO NOT ADMINISTER AS IV PUSH OR BOLUS**
- Premedicate with Acetaminophen 650mg PO (2 tabs) & Diphenhydramine 50mg PO before each dose

COMPLETE TREATMENT IN 4 CYCLES ONLY

RITUXIMAB DOSAGE PREPARATION (at 3mg/mL):

BSA (mg/m ²)	Dose (mg)	Dose (mL)	Diluent (mL)	Total Volume (mL)
1.3	488	49	114	163
1.4	525	53	124	177
1.5	563	56	131	187
1.6	600	60	140	200
1.7	638	64	149	213
1.8	675	68	159	227
1.9	713	71	166	237
2.0	750	75	175	250
2.1	788	79	184	263
2.2	825	83	194	277

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

RITUXIMAB DRUG INFUSION RATES (at 3mg/mL):

DOSAGE RATE (mg/hr)	INFUSION RATE (mL/hr)
50	17
100	33
150	50
200	67
250	83
300	100
350	117
400	133

GUIDELINE

See the CCNS website
www.cancercare.ns.ca for the
guideline on Rituximab for lymphoma

LY

LY-RITUX

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic before chemotherapy
- After chemotherapy, may use a Dopamine Receptor Antagonist PRN ((Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10mg PO q4h PRN) or no antiemetic therapy

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

HYPOTENSION PROPHYLAXIS

- Patient should hold any antihypertensive medications for 12 hours before each dose of Rituximab

CLINICAL MONITORING

- Close observation for **infusion-related symptoms**, including fever, chills, pain (including pain in tumour), asthenia, and other flu-like symptoms. If treatment is well-tolerated during loading dose and early maintenance doses, observation times may be reduced.
- Clinical **cardiac monitoring** for all patients with cardiac risk factors or previous cardiac conditions (incl. arrhythmias, angina)
- Observe for **symptoms of hypersensitivity**, including hypotension, bronchospasm or angioedema

HYPERSENSITIVITY

0. None
1. Transient rash; fever $<38^{\circ}\text{C}$
2. Urticaria; fever $\geq 38^{\circ}\text{C}$; bronchospasm
3. Serum sickness, bronchospasm, requires parenteral medications
4. Anaphylaxis

Rated at each clinic visit

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:

Approximately 1-3 hours (On the first visit- Approx. 4-8 hours)

LY-RITUX-CHOP

Rituximab plus Cyclophosphamide-Doxorubicin- Vincristine- Prednisone (CHOP) Chemotherapy

(Treatment of Low-Grade
or Follicular B-cell Non-Hodgkin's
Lymphoma which is CD-20 Positive in
patients ≥ 60 years old)

**ADVANCED LEVEL REGIMEN (First
Cycle)-** Provincial Cancer Centre

**INTERMEDIATE LEVEL REGIMEN
(Subsequent cycles- if no reaction)-**
Regional Hospital with Dedicated
Cancer Treatment Unit

RITUXIMAB 375mg/m² IV Days 1, 8, 15 & 22 Only

- Infuse IV at 50mg/hr, then increase by increments of 50mg/hr every 30 minutes, as tolerated, to a final rate of 400mg/hr for the first dose
- Subsequent infusions may be initiated at 100mg/hr and increased by increments of 100mg/hr every 30 minutes to the maximum rate of 400mg/hr, as tolerated by the patient
- Observe for 30-60 minutes after infusion
- Infusion-related symptoms may be managed by slowing or interrupting the infusion, and with the use of supportive care (including IV saline, acetaminophen, diphenhydramine, or bronchodilators, as needed)
- Mix in Normal Saline to designated volume for dose- Table of volumes and infusion rates for 2mg/mL; may dilute to final concentration of 1-4mg/mL
- **DO NOT ADMINISTER AS IV PUSH OR BOLUS**
- Premedicate with **Acetaminophen 650mg PO (2 tabs) & Diphenhydramine 50mg PO** before each dose

COMPLETE TREATMENT IN 4 CYCLES ONLY

DOXORUBICIN 50mg/m² IV Day 1 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV; Give over at least 3-5 minutes

VINCRIStINE 1.4mg/m² IV Day 1

- Push through sidearm of free flowing IV; Inject over at least 1 minute

CYCLOPHOSPHAMIDE 750mg/m² IV Day 1 (Round to nearest 10mg)

- Mix in 250mL bag (Normal Saline); Infuse over 30 minutes

PREDNISONE 150mg PO for 5 days

(Outpatient prescription in multiples of 50mg tablets)

REPEAT EVERY 21 DAYS

For a Usual Total of 6 to 8 Cycles

LY

LY-RITUX-CHOP

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK- CHOP Chemotherapy Cycles

Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO/IV (i.e. Ondansetron 8-16mg PO or 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), and
- Dexamethasone 20mg IV
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO)
"When available in Canada"

Post-Chemotherapy-

- Dexamethasone 8 mg PO twice daily for 2 to 3 days, and
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *"When available in Canada"*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration (to prevent renal toxicity)

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

RITUXIMAB DOSAGE PREPARATION

(at 3mg/mL):

BSA (mg/m ²)	Dose (mg)	Dose (mL)	Diluent (mL)	Total Volume (mL)
1.3	488	49	114	163
1.4	525	53	124	177
1.5	563	56	131	187
1.6	600	60	140	200
1.7	638	64	149	213
1.8	675	68	159	227
1.9	713	71	166	237
2.0	750	75	175	250
2.1	788	79	184	263
2.2	825	83	194	277

RITUXIMAB DRUG INFUSION RATES

(at 3mg/mL):

DOSAGE RATE (mg/hr)	INFUSION RATE (mL/hr)
50	17
100	33
150	50
200	67
250	83
300	100
350	117
400	133

Continued Next Page...

CLINICAL MONITORING

Rituximab Treatment visits:

- Close observation for **infusion-related symptoms**, including fever, chills, pain (including pain in tumour), asthenia, and other flu-like symptoms. If treatment is well-tolerated during loading dose and early maintenance doses, observation times may be reduced.
- Clinical **cardiac monitoring** for all patients with cardiac risk factors or previous cardiac conditions (incl. arrhythmias, angina)
- Observe for **symptoms of hypersensitivity**, including hypotension, bronchospasm or angioedema

HYPERSENSITIVITY

0. None

1. Transient rash, fever $<38^{\circ}\text{C}$
2. Urticaria, fever $\geq 38^{\circ}\text{C}$, bronchospasm
3. Serum sickness, bronchospasm, requires parenteral medications
4. Anaphylaxis

Rated at each clinic visit

CHOP Chemotherapy Cycles

- **Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes** before each cycle of treatment
- Baseline **renal function tests** (if failure suspected) [serum creatinine, electrolytes & BUN] & **liver function tests** (especially if poor Performance Status) (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated)
- **Serum glucose** levels (monitor routinely for diabetic patients)
- Periodic **urinalysis (RBCs)** and in response to patient complaint
- **Neurologic toxicity** ratings at each visit
- Clinical exam for symptoms of **Congestive Heart Failure**
- Periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels

CONSTIPATION

0. No change
1. Mild
2. Moderate
3. Severe
4. Ileus >96 hours

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss; moderate paraesthesia
3. Sensory loss interferes with function

Rated at each clinic visit

LY

LY-RITUX-CHOP

DOSE MODIFICATION

CHOP Chemotherapy Cycles

Hematologic Toxicities

1. If ANC $< 1.0 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, **HOLD** dose for 1 week (Until ANC $\geq 1.0 \times 10^9/L$)

Renal failure

1. If Serum Creatinine $> 265 \mu\text{mol/L}$, reduce Doxorubicin to **50%** dose
2. If CrCl $< 12 \text{ mL/min}$, **OMIT** Cyclophosphamide dose (Suggested action)

Hepatic dysfunction

1. If Bili = $26-51 \mu\text{mol/L}$ or AST = $60-180 \text{ IU/L}$, reduce Doxorubicin to **75%** dose, and Vincristine to **50%** dose
2. If Bili = $52-85 \mu\text{mol/L}$ or AST $> 180 \text{ IU/L}$, reduce Cyclophosphamide to **75%** dose, Doxorubicin to **50%** dose and Vincristine to **25%** dose
3. If Bili $> 85 \mu\text{mol/L}$, **OMIT** ALL drugs (Suggested action)

GUIDELINE

See the CCNS website
www.cancercare.ns.ca for the
guideline on Rituximab for lymphoma

NOTE

The guideline on Rituximab for lymphoma has been revised to include the combination regimen Ritux-CHOP as an option for eligible patients (diffuse large cell lymphoma). At present, Ritux-CHOP continues to require a non-formulary approval.

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:

Rituximab Treatment Visits:

Approximately 1-3 hours

(On the first visit- Approx. 4-8 hours)

Confirm Appt. Type with Chemo Nurse
CHOP Chemotherapy Visits: Approx. 2 hours

REGIMEN CONTENTS

ME-CCD - *Carmustine-Cisplatin-
Dacarbazine Chemotherapy*

ME-DACARB - Dacarbazine
Chemotherapy 468

ME-IFN*I - Interferon Induction
Therapy 469

ME-IFN*M - Interferon Maintenance
Therapy 470

ME-TEMOZOL - Temozolomide
Chemotherapy 471

ME

NOTE: *Regimen names in italics are not in this pocketbook version- See full version for regimen monograph*

ME-DACARB

Dacarbazine Chemotherapy

(Malignant Melanoma)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

DACARBAZINE 200mg/m² IV Days 1 to 5

May give **300-350mg/m²** IV Days 1 to 3

- Mix in 250mL bag (Normal Saline); Infuse through main IV line, with an additional 500mL Normal Saline run at same time by piggyback, to reduce vein irritation (more IV fluid if ordered)
- Infuse over 60 minutes; If vein irritation, infuse slowly
- **PROTECT FROM LIGHT** (Round to nearest 10mg)

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO) **When available in Canada**

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
- No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
- Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) **When available in Canada**
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)

CLINICAL MONITORING

Hematologic Toxicities

1. If ANC < $1.5 \times 10^9/L$, or if Platelets < $125 \times 10^9/L$, on Day 1, notify physician and **HOLD** dose for 5-7 days
2. If ANC < $0.5 \times 10^9/L$, or if Platelets < $75 \times 10^9/L$, at Day 22, notify physician and **HOLD** dose for 1 week

Renal failure

1. If CrCl < 60mL/min, reduce dose of Dacarbazine by 25-50%
(Suggested action)

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:
Approx. 2½ hours

[Rev 11/01]

ME-IFN*I

Interferon Induction Therapy

(High Risk Malignant Melanoma)

INTERMEDIATE LEVEL REGIMEN-

Regional Hospital with Dedicated
Cancer Treatment Unit

INTERFERON ALFA 20MU/m² IV Days 1 to 5 each week for 4 weeks

- Mix each dose in 100mL minibag (Normal Saline); administer over 20 minutes
- ACETAMINOPHEN 650mg (2 tabs) before each dose

INITIAL CYCLE OF 28 DAYS

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC), liver function tests (Serum alkaline phosphatase, GGT, ALT, AST & Bilirubin) and serum glucose levels twice weekly

LETHARGY

0. None
1. Mild (Performance Status decreased by 1)
2. Moderate (Performance Status decreased by 2)
3. Severe (Performance Status decreased by 3)

Rated at weekly clinic visit

FLU-LIKE SYMPTOMS

0. None
1. Mild
2. Moderate
3. Severe

*(Arthralgia, myalgia,
diaphoresis, rigours/
chills)*

DOSE MODIFICATION CRITERIA

LEVEL I TOXICITY:

- ANC = 0.25 TO $<0.5 \times 10^9/L$
- PLT 25 to $50 \times 10^9/L$
- AST > 5 to $10 \times$ Normal ($>175-350U/L$)
- Bilirubin 1.5 to $2 \times$ Normal ($>27-36\mu mol/L$)
- Lab tests twice weekly
- **HOLD** Interferon until toxicity less than Level I severity. Then resume at 50% full dose

LEVEL II TOXICITY:

- ANC $< 0.25 \times 10^9/L$
- PLT $< 25 \times 10^9/L$
- AST $> 10 \times$ Normal ($>350U/L$)
- Bilirubin $> 2.1 \times$ Normal ($>37\mu mol/L$)
- Lab tests twice weekly
- **DISCONTINUE** Interferon

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:

Approx. 30 minutes/day

ME

ME-IFNM***

**Interferon Maintenance
Therapy**

**Take-Home Prescription-
Special Authorization Required**

(High Risk Malignant Melanoma- Following Induction Therapy)

INTERFERON ALFA 10MU/m² SC Monday, Wednesday & Friday (three times weekly) for 48 weeks

Drug available by retail prescription: subcutaneous self-administration (or administered by home caregiver)

ACETAMINOPHEN 650mg (2 tabs) before each dose

SUBSEQUENT CYCLES OF 28 DAYS

For a Usual Total of 48 weeks

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC), liver function tests (Serum alkaline phosphatase, GGT, ALT, AST & Bilirubin) and serum glucose levels twice weekly

LETHARGY

0. None
1. Mild (Performance Status decreased by 1)
2. Moderate (Performance Status decreased by 2)
3. Severe (Performance Status decreased by 3)

FLU-LIKE SYMPTOMS

0. None
1. Mild
2. Moderate
3. Severe

Rated at weekly clinic visit

(Arthralgia, myalgia, diaphoresis, rigours/chills)

DOSE MODIFICATION CRITERIA

LEVEL I TOXICITY:

- ANC= 0.25 TO $<0.5 \times 10^9/L$
- PLT 25 to $50 \times 10^9/L$
- AST > 5 to $10 \times$ Normal ($>175-350U/L$)
- Bilirubin 1.5 to $2 \times$ Normal ($>27-36\mu\text{mol/L}$)
- Lab tests twice weekly
- **HOLD** Interferon until toxicity less than Level I severity. Then resume at 50% full dose

LEVEL II TOXICITY:

- ANC $< 0.25 \times 10^9/L$
- PLT $<25 \times 10^9/L$
- AST $>10 \times$ Normal ($>350U/L$)
- Bilirubin $>2.1 \times$ Normal ($>37\mu\text{mol/L}$)
- Lab tests twice weekly
- **DISCONTINUE** Interferon

NOTE

Prescription costs covered by most third party prescription plans; for Pharmacare approval the prescriber must write a letter of request for each patient

ME

ME-TEMOZOL

Temozolomide Chemotherapy

(CNS Metastases from Malignant
Melanoma- Palliative Intent)

Take-Home Prescription-
Special Authorization Required

TEMOZOLOMIDE 150mg/m² PO Days 1 to 5

Increase to 200mg/m² PO days 1-5 if no myelosuppression at Day 22 nadir
(Outpatient prescription in multiples of 5mg, 20mg, 100mg & 250mg capsules)

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: INTERMEDIATE RISK

- Ondansetron 8mg PO & Dexamethasone 8-20mg PO before each oral chemo dose, days 1 to 5 (*eliminate Dexamethasone if steroids already in use*)
- Ondansetron 8mg PO & Dexamethasone 8mg PO 12 hours after each oral dose & q12h for 2-3 days after last chemo treatment (total of 14-16 doses, at 12 hour intervals, from start)
- *If vomiting not controlled during first treatment cycle, substitute for alternate setron antiemetic (use Dolasetron or Granisetron PO) or escalate antiemetic treatment doses- Vomiting may increase Intracranial Pressure with larger brain tumours*

CLINICAL MONITORING

NO RECOMMENDED TOXICITY
RATINGS

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.0×10^9 /L or if Platelets < 50×10^9 /L during any cycle, the next cycle must be reduced

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

NOTES

- Prescription costs covered by some third party prescription plans; for Pharmacare approval the prescriber must write a letter of request for each patient (Note: This indication is NOT covered in the guideline for Temozolomide, often used by Pharmacare to determine coverage)
- The cost per treatment course (i.e. 14 days) can range from \$1,000-1,500, depending upon patient size

REGIMEN CONTENTS

MY-BORTEZ - <i>Bortezomib</i> (Velcade®) <i>Monotherapy</i>	
MY-CYCLO*IV - Cyclophosphamide*IV Chemotherapy	473
MY-CYCLO*PO - Cyclophosphamide* PO Chemotherapy	474
MY-DCEP - Dexamethasone- Cyclophosphamide-Etoposide Cisplatin (DCEC) Chemotherapy	475
MY-DEXA*PO - Dexamethasone*PO Chemotherapy	477
MY-IFN*M - <i>Interferon Maintenance Therapy</i>	
MY-MELPH*IV - <i>Melphalan IV Chemotherapy</i>	
MY-MELPH-PRED - Melphalan- Prednisone Chemotherapy	478
MY-PAMID - Pamidronate Therapy	479
MY-THALID - <i>Thalidomide Therapy</i>	
MY-VAD - Vincristine-Doxorubicin- Dexamethasone (VAD) Chemotherapy	480

NOTE: *Regimen names in italics are not in this pocketbook version- See full version for regimen monograph*

MY-CYCLO*IV

Cyclophosphamide*IV Chemotherapy

(Multiple Myeloma- Palliative Intent)

BASIC LEVEL REGIMEN-
Community Hospital with
Oncology Nurses

CYCLOPHOSPHAMIDE 300mg IV Weekly

(May be given as 1000mg/m² IV every 28 days) (Round to nearest 10mg)

• Mix in 250mL bag (Normal Saline); Infuse over 30 minutes

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: INTERMEDIATE RISK

Pre-Chemotherapy-

- Dopamine Receptor Antagonist PO (Prochlorperazine 10mg PO or Metoclopramide 10-20mg PO), **AND**
- Dexamethasone 8mg PO

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Dopamine Receptor Antagonist PRN ((Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10mgPO q4h PRN)
- *Oral hydration is strongly encouraged. poorly hydrated patients may need more IV hydration (to prevent renal toxicity)*

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes before each cycle of treatment
- Urinalysis (RBCs)- routine for high intravenous doses (>1000mg/m²); periodic for low IV dose/and in response to patient complaint
- Baseline renal function tests (if failure suspected) [serum creatinine, electrolytes & BUN]

NOTE

- Cytotoxic treatment of myeloma should be accompanied by Pamidronate therapy
- See MY-PAMID; Pamidronate may be administered at the same visit as the chemotherapy, or may be given on a separate schedule

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.0 x 10⁹/L, or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Hepatic dysfunction (Suggested action)

1. If Bili = 51-85µmol/L or AST > 180IU/L, reduce Cyclophosphamide to **75%** dose
2. If Bili > 85µmol/L, **Omit** Cyclophosphamide

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:
Approx. 30-45 minutes

MY

MY-CYCLO*PO**Cyclophosphamide*PO
Chemotherapy***(Multiple Myeloma- Palliative Intent)***Take-Home Prescription-
Unrestricted**

CYCLOPHOSPHAMIDE 50-200mg PO daily for 14 days
(Outpatient prescription in multiples of 25mg & 50mg tablets)

REPEAT EVERY 28 DAYS**SUPPORTIVE CARE****ANTIEMETIC REGIMEN: LOW RISK**

- Prochlorperazine 10mg PO (and/or PR) q4-6h PRN or Metoclopramide 10mgPO q3-4h PRN

DOSE MODIFICATIONHematologic Toxicities

1. If ANC $< 1.0 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, **HOLD** dose for 1 week

Hepatic dysfunction (Suggested action)

1. If Bili = $51-85\mu\text{mol/L}$ or AST $> 180\text{IU/L}$, reduce Cyclophosphamide to 75% dose
2. If Bili $> 85\mu\text{mol/L}$, **Omit** Cyclophosphamide

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes before each cycle of treatment
- Baseline renal function tests (if failure suspected) [serum creatinine, electrolytes & BUN]
- Periodic urinalysis (RBCs) and in response to patient complaint

NOTE

Cytotoxic treatment of myeloma should be accompanied by Pamidronate therapy

- See MY-PAMID. Pamidronate may be administered at the same visit as the chemotherapy, or may be given on a separate schedule

MY-DCEP

Dexamethasone- Cyclophosphamide- Etoposide-Cisplatin Chemotherapy

(Multiple Myeloma- Salvage Therapy)

ADVANCED LEVEL REGIMEN-
Provincial Cancer Centre

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with
Hematologist Supervision

DEXAMETHASONE 40mg/m² PO for Days 1 to 4

(Outpatient prescription in multiples of 4mg tablets)

CYCLOPHOSPHAMIDE 300mg/m² IV Days 1 to 4

(Total Dose = 1200mg/m² over 96 Hours) (Round to nearest 10mg)

ETOPOSIDE 30mg/m² CIV Days 1 to 4

(Total Dose = 120mg/m² over 96 Hours) (Round to nearest 10mg)

CISPLATIN 15mg/m² CIV Days 1 to 4

(Total Dose = 60mg/m² over 96 Hours) (Round to nearest 1mg)

- Admix daily doses of Cyclophosphamide, Etoposide & Cisplatin together in 1000mL bag of Normal Saline. Infuse over 24 hours, Repeat daily for a total of 4 days (96 hours)
- May be given by continuous ambulatory infusion using a CADD pump in IV bag or ambulatory pump cassette

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy: Daily for 4 days

- Serotonin Receptor Antagonist PO- Ondansetron 8mg PO pre-chemo and q12h for 8 doses on Days 1 to 4, (or Granisetron 1mg PO pre-chemo and q24h for 4 doses days 1 to 4, or Dolasetron 100mg PO pre-chemo and q24h for 4 doses days 1 to 4)

Post-Chemotherapy:

- Serotonin Receptor Antagonist PO- Ondansetron 8mg PO q12h for 2 doses on Day 5 (if given prechemo) **OR**
- No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
- Granisetron 2mg PO q24h for 1 dose on Day 5, or Dolasetron 100mg PO q24h for 1 dose on Day 5, if given pre-chemo)

OTHER SUPPORTIVE CARE

- Famcyclovir 250-500mg PO q12h, Ciprofloxacin 500mg PO q12h & Fluconazole 400mg PO daily until AGC >0.5 x 10³/L for 2 consecutive days
- Ranitidine 150mg PO bid
- Filgrastim 5mcg/kg SC daily for 7 days (or until ANC >2 x 10³/L for 2 consecutive days, starting 72 hours after the completion of chemotherapy (300µg for patients ≤60Kg, 480µg for patients >60Kg)
- Oral hydration is strongly encouraged: poorly hydrated patients may need more IV hydration (to prevent renal toxicity)

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

Continued Next Page...

MY-DCEP

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes before cycle of treatment
- Baseline and routine renal function tests [serum creatinine & BUN]- especially if there are other concurrent nephrotoxic drugs
- Hearing & Neurologic toxicity ratings (Sensory) each visit; hearing tests if symptomatic
- Periodic liver function tests (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated)
- Clinical assessment of stomatitis; oral examination upon patient complaint of a sore mouth; clinical exam for proximal muscle myopathy
- Urinalysis (RBCs)- periodic for low IV dose/and in response to patient complaint
- Serum glucose levels (for diabetic patients on multiple day treatments)

HEARING

0. No change
1. Asymptomatic
2. Tinnitus
3. Correctable hearing loss
4. Deafness

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss; moderate paraesthesia
3. Sensory loss interferes with function

Rated at each clinic visit

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < $1.0 \times 10^9/L$, or if Platelets < $100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week (Until ANC $\geq 1.5 \times 10^9/L$)

Renal failure

1. If CrCl= 30-60mL/min or Serum Creatinine=136-185 μ mol/L, reduce Cisplatin to **50%** dose, and Etoposide to **75%** dose
2. If CrCl< 30mL/min or Serum Creatinine>185 μ mol/L, **Omit** Cisplatin
3. If Serum Creatinine >265 μ mol/L, reduce Doxorubicin to **50%** dose
4. If CrCl < 12mL/min, reduce Etoposide to **50%** dose and **OMIT** Cyclophosphamide dose (*Suggested action*)

Hepatic dysfunction (*Suggested action*)

1. If Bili=26-51 μ mol/L or AST =60-180IU/L, reduce Doxorubicin to **75%** dose and Etoposide to **50%** dose
2. If Bili= 52-85 μ mol/L or AST>180IU/L, reduce Cyclophosphamide to **75%** dose, Doxorubicin to **50%** dose and
3. If Bili > 85 μ mol/L, **OMIT** ALL drugs

NOTE

Cytotoxic treatment of myeloma should be accompanied by Pamidronate therapy

- See MY-PAMID, Pamidronate may be administered at the same visit as the chemotherapy, or may be given on a separate schedule

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

[Rev 11/01]

MY-DEXA*PO**Dexamethasone*PO
Chemotherapy***(Multiple Myeloma)***DEXAMETHASONE 40mg** PO for 4 days

Days 1 to 4, 9 to 12 & 17 to 21 (Outpatient prescription in multiples of 4mg tablets)

**Take-Home Prescription-
Unrestricted****REPEAT EVERY 28 DAYS****SUPPORTIVE CARE****ANTIEMETIC REGIMEN: NONE****DOSE MODIFICATION**Hematologic Toxicities

1. If ANC $< 1.0 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

CLINICAL MONITORING

- Serum glucose levels (for diabetic patients on multiple day treatments)
- Clinical exam for **proximal muscle myopathy**

NOTE

Cytotoxic treatment of myeloma should be accompanied by Pamidronate therapy

- See MY-PAMID; Pamidronate may be administered at the same visit as the chemotherapy, or may be given on a separate schedule

MY

MY-MELPH-PRED

Melphalan-Prednisone Chemotherapy

(Multiple Myeloma)

Take-Home Prescription-
Unrestricted

MELPHALAN 9mg/m² PO Days 1 to 4

(Outpatient prescription in multiples of 2mg tablets)

PREDNISONE 100mg PO Days 1 to 4

(Outpatient prescription in multiples of 50mg tablets)

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE
ANTIEMETIC REGIMEN: NONE

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.0 x 10⁹/L, or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC), serum electrolytes and serum uric acid levels before each cycle of treatment
- Serum glucose levels (for diabetic patients)

NOTE

Cytotoxic treatment of myeloma should be accompanied by Pamidronate therapy

- See MY-PAMID; Pamidronate may be administered at the same visit as the chemotherapy, or may be given on a separate schedule

MY-PAMID

Pamidronate Therapy

*(Prevention of Skeletal Events
(Pathologic Fractures), Bony Pain,
and Radiotherapy to the Bones-
Associated with Multiple Myeloma)*

BASIC LEVEL REGIMEN-
Community Hospital with
Oncology Nurses

PAMIDRONATE 90mg IV over 2 hours (or longer)

Administer concurrently with first-line or salvage cytotoxic chemotherapy

- Mix in 500mL solution (5% Dextrose, Normal Saline) and infuse over 4 hours for first dose (if observation required); subsequent infusions may be given over 2 to 2½ hours, unless serum creatinine >260µmol/L- then continue with 4 hour infusion time
- Admix into 250mL ambulatory pump & infuse over 2-5 hours at home for subsequent doses (e.g. Intermate LV 50 pump- 250mL at 50 mL/hr)

REPEAT EVERY 28 DAYS

DOSE MODIFICATION

1. If Corrected Serum Calcium* <2.10µmol/L, notify physician and **HOLD** dose for 1 week, or until Serum Calcium levels within normal range
2. If serum creatinine >260µmol/L, adjust infusion to longer time (4 hours)

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

CLINICAL MONITORING

- **Renal function tests** (if failure suspected) [serum creatinine, electrolytes & BUN] at baseline and before each treatment cycle
- **Serum electrolytes**, including **serum calcium**, and **serum creatinine** before each dose

HYPOCALCEMIA

0. Serum Calcium >2.10 µmol/L
1. Serum Calcium =2.10 to 1.93 µmol/L
2. Serum Calcium =1.92 to 1.74 µmol/L
3. Serum Calcium =1.73 to 1.51 µmol/L
4. Serum Calcium <1.50 µmol/L

Rated on assessment of anti-hypercalcemia response and at periodic visits or in response to patient complaint

*Corrected Serum Calcium = Measured Serum Calcium + [(40 - Serum Albumin) x 0.02]

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:
Approximately 4 hours OR: 15 minutes for ambulatory pump

MY

**MY-VAD****Vincristine-Doxorubicin-Dexamethasone (VAD) Chemotherapy***(Multiple Myeloma)***INTERMEDIATE LEVEL REGIMEN-**Regional Hospital with
Hematologist Supervision**VINCRIStINE 0.4mg/day** CIV for Days 1 to 4(Total Dose = $1.6\text{mg}/\text{m}^2$ over 96 Hours) (Round to nearest 0.1mg)**DOXORUBICIN 9mg/m²/day** CIV for Days 1 to 4(Total Dose = $36\text{mg}/\text{m}^2$ over 96 Hours) (Round to nearest 1mg)

- Admix daily doses of Vincristine & Doxorubicin together into 1000mL bag (Normal Saline); Infuse over 24 hours, repeat daily for 4 days (*Inpatient Treatment*) OR
- Admix total doses of Vincristine & Doxorubicin together with Normal Saline to 192mL total volume; Infuse over 96 hours via Infusor Pump (2mL/hr) (*Outpatient Treatment*)
- May be given by continuous ambulatory infusion using a CADD pump in IV bag or ambulatory pump cassette
- Infuse through a central venous catheter

DEXAMETHASONE 40mg PO for 4 days- Days 1-4, 9-12 & 17-20

(Outpatient prescription in multiples of 4mg tablets)

REPEAT EVERY 28 DAYS**SUPPORTIVE CARE****ANTIEMETIC LOW RISK**

- Metoclopramide 20mg IV/PO before chemotherapy on Day 1 ONLY
- After chemotherapy, use Metoclopramide 10-20mg PO/IV & Diphenhydramine 25-50mg PO/IV q4h PRN for breakthrough nausea, OR Prochlorperazine 10mg PO q4-6h PRN

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN****DOSE MODIFICATION**Hematologic Toxicities

1. If ANC $< 1.0 \times 10^9/\text{L}$, or if Platelets $< 100 \times 10^9/\text{L}$, notify physician and **HOLD** dose for 1 week

Renal failure (*Suggested action*)

1. If Serum Creatinine $> 265\mu\text{mol}/\text{L}$, **reduce** Doxorubicin to **50%** dose
- Hepatic dysfunction (*Suggested action*)

1. If Bili= $25\text{--}50\mu\text{mol}/\text{L}$ or AST= $60\text{--}180\text{IU}/\text{L}$, **reduce** Doxorubicin and Vincristine to **50%** dose
2. If Bili= $51\text{--}85\mu\text{mol}/\text{L}$ or AST $>180\text{IU}/\text{L}$, **reduce** Doxorubicin and Vincristine to **25%** dose
3. If Bili $> 85\mu\text{mol}/\text{L}$, **Omit** Doxorubicin dose

Continued Next Page...

MY-VAD

CLINICAL MONITORING

- **Complete blood count** including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- **Neurologic** toxicity ratings (Sensory, Constipation) at each visit
- Clinical exam for symptoms of **Congestive Heart Failure**
- Periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels
- Baseline **liver function tests** (especially if poor Performance Status) (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated)
- **Serum glucose levels** (for diabetic patients on multiple day treatments)
- Clinical exam for **proximal muscle myopathy**

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss; moderate paraesthesia
3. Sensory loss interferes with function

CONSTIPATION

0. No change
1. Mild
2. Moderate
3. Severe
4. Ileus >96 hours

Rated at each clinic visit

NOTE

Cytotoxic treatment of myeloma should be accompanied by Pamidronate therapy

• See MY-PAMID: Pamidronate may be administered at the same visit as the chemotherapy is prescribed, or may be given on a separate schedule

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:

Day 1 = Approx. 30 minutes

Day 5 = 15 to 30 minutes

REGIMEN CONTENTS

NE-CARBO-ETOP - Carboplatin-
Etoposide Chemotherapy 483

NE-CISP-ETOP - Cisplatin-Etoposide
Chemotherapy 485

NE-CYTAR*HD - *High Dose*
Cytarabine Chemotherapy

NE-IFOS-CARBO-ETOP -
Ifosfamide-Carboplatin-Etoposide
Chemotherapy 487

NE-L-CARBO-V - Lomustine-
Carboplatin-Vincristine
Chemotherapy 490

NE-LCV - Lomustine-Cisplatin-
Vincristine Chemotherapy 493

NE-LOMUST - Lomustine
Chemotherapy 495

NE-MVP*HD - *High Dose*
Methotrexate-Vincristine-
Procarbazine

NE-PLV - Procarbazine-Lomustine-
Vincristine (PCV) Chemotherapy 496

NE-TEMOZOL - Temozolomide
Chemotherapy 498

NOTE: *Regimen names in italics are not in this pocketbook version- See full version for regimen monograph*

NE-CARBO-ETOP

Carboplatin-Etoposide Chemotherapy

(Adjuvant Treatment of Glioma,
Oligodendroglioma)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

ETOPOSIDE 100mg/m²IV Days 1 to 3 (Round to nearest 10mg)

- Premixed in 500mL bags of Normal Saline; connect piggyback to IV line; Infuse over 60 minutes; Adjust rate if blood pressure drops

CARBOPLATIN AUC= 6 mg/mL/min IV Day 1 (Round to nearest 5mg)

- Mix in 250mL bag (5% Dextrose); Infuse over 30 minutes

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO prechemo each day (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV- pre-chemo & 8mg PO qhs on Days 1 to 3 **OR**
 - Granisetron 2mg PO or 1mg IV prechemo each day; **OR** Dolasetron 100mg PO or 100mg IV prechemo each day), **AND**
- Dexamethasone 8mg PO prechemo each day (may increase to 20mg PO or IV)- *OMIT Dexamethasone if patient is already taking ≥ 16 mg per day.* **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO) *"When available in Canada"*

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses- *OMIT Dexamethasone if patient is already taking ≥ 16 mg per day.* **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo, **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *"When available in Canada"*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

NE

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NE-CARBO-ETOP

CLINICAL MONITORING

- **Complete blood count** including differential, platelets and hemoglobin (CBC) and serum electrolytes before each cycle of treatment
- **Neurologic** toxicity ratings (Sensory) at each visit
- Baseline and periodic **renal function tests** [serum creatinine, electrolytes & BUN]; **serum creatinine** level before each cycle of chemotherapy
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- Baseline **blood pressure** at each treatment; monitor for hypotension

SENSORY

0. No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss; moderate paraesthesia
3. Sensory loss interferes with function

Rated at each clinic visit

NOTE

Calvert AUC Dosing Formula

DOSE (mg)=target AUC x (GFR + 25)

- GFR expressed as measured Creatinine clearance (mL/min) or estimated from serum Creatinine Creatinine Clearance (X60 for mL/min)

$$Cl_{Cr} \text{ (mL/sec)} = \frac{140 - \text{age (yrs)}}{72} \times \frac{\text{TBW (kg)}}{Cr_{\text{serum}} \text{ (}\mu\text{mol/L)}}$$

$$Cl_{Cr} \text{ (mL/sec)} = Cl_{Cr} \text{ (mL/min)} \times 0.85$$

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < $1.5 \times 10^9/L$, notify physician and **HOLD** dose (Until ANC $\geq 1.5 \times 10^9/L$)

Renal failure (Recommended action)

1. If Serum Creatinine = 136-150 $\mu\text{mol/L}$ or Creatinine Clearance = 40-60 mL/min; **reduce** Carboplatin dose by **1mg/mL/min** (or by **50mg/m²** for BSA dosing)
2. If Serum Creatinine = 151-180 $\mu\text{mol/L}$ or Creatinine Clearance = 20-40 mL/min; **reduce** Carboplatin dose by **2mg/mL/min** (or by **100mg/m²** for BSA dosing)
3. If Serum Creatinine > 181 $\mu\text{mol/L}$ or Creatinine Clearance < 20 mL/min, **OMIT** Carboplatin dose
4. If CrCl < 12 mL/min, reduce Etoposide to **50% dose**

Hepatic dysfunction (Suggested action)

1. If Bili = 26-51 $\mu\text{mol/L}$ or AST = 60-180 IU/L, reduce Etoposide to **50% dose**
2. If Bili = 52-85 $\mu\text{mol/L}$, reduce Etoposide to **25% dose**

PATIENT VISIT

CHEMOTHERAPY VISIT:

Approx. 2 hours/day

NE-CISP-ETOP

Cisplatin-Etoposide

Chemotherapy

(Adjuvant Treatment of Glioma,
Oligodendroglioma)

INTERMEDIATE LEVEL REGIMEN-

Regional Hospital with Dedicated
Cancer Treatment Unit

PREHYDRATION

- Encourage patient to drink 6-8 glasses of water prior to chemo each day
- May prehydrate with 500mL Normal Saline; Infuse over 60 minutes Days 1 to 3

ETOPOSIDE 100 mg/m² IV Days 1 to 3 (Round to nearest 10mg)

- Premixed in 500mL bags of Normal Saline; connect piggyback to IV line; Infuse over 60 minutes; Adjust rate if blood pressure drops
- Give Etoposide BEFORE Cisplatin, to hydrate patient

CISPLATIN 30 mg/m² IV Days 1 to 3 (Round to nearest 1mg)

- Mix drug in 250mL bag (Normal Saline); Infuse over 60 minutes; May also admix 10G Mannitol (100mL of 10% solution) with Cisplatin

POSTHYDRATION

- May give 500mL Normal Saline if additional hydration needed; Infuse over 60 minutes Days 1-3

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO prechemo each day (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV- pre-chemo & 8mg PO qhs on Days 1 to 3 **OR**
 - Granisetron 2mg PO or 1mg IV prechemo each day; **OR** Dolasetron 100mg PO or 100mg IV prechemo each day), **AND**
- Dexamethasone 8mg PO prechemo each day (may increase to 20mg PO or IV)- *OMIT Dexamethasone if patient is already taking ≥ 16 mg per day*, **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO) *"When available in Canada"*

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses- *OMIT Dexamethasone if patient is already taking ≥ 16 mg per day*, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo, **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *"When available in Canada"*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

Continued Next Page...

NE-CISP-ETOP

CLINICAL MONITORING

- **Complete blood count** including differential, platelets and hemoglobin (CBC) and serum electrolytes [including Mg^{2+}] before each cycle of treatment
- **Renal function tests** [serum creatinine & BUN] before each cycle of chemotherapy
- **Liver function** [Bilirubin levels] checked before each cycle of treatment
- **Clinical assessment of stomatitis**; oral examination upon patient complaint of a sore mouth
- **Hearing & Neurologic toxicity ratings** (Sensory)- each visit

HEARING

- 0 No change
- 1. Asymptomatic
- 2. Tinnitus
- 3. Correctable hearing loss
- 4. Deafness

SENSORY

- 0. No change
- 1. Mild paraesthesia; no deep tendon reflex
- 2. Mild/moderate sensory loss; moderate paraesthesia
- 3. Sensory loss interferes with function

Rated at each clinic visit

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

DOSE MODIFICATION

Hematologic Toxicities

1. If $ANC < 1.5 \times 10^9/L$, or if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose (Until $ANC \geq 1.5 \times 10^9/L$)

Renal failure (Recommended action)

1. If $CrCl = 30-60 mL/min$ or Serum Creatinine $= 136-185 \mu mol/L$, reduce Cisplatin to **50%** dose, and Etoposide to **75%** dose
2. If $CrCl < 30 mL/min$ or Serum Creatinine $> 185 \mu mol/L$, **Omit** Cisplatin dose
3. If $CrCl < 12 mL/min$, reduce Etoposide to **50%** dose

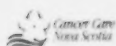
Hepatic dysfunction (Suggested action)

1. If $Bili = 26-51 \mu mol/L$ or $AST = 60-180 IU/L$, reduce Etoposide to **50%** dose
2. If $Bili = 52-85 \mu mol/L$, reduce Etoposide to **25%** dose
3. If $Bili > 85 \mu mol/L$ or $AST > 180 IU/L$, **Omit** Etoposide

PATIENT VISIT

CHEMOTHERAPY VISIT

Approx. 2 hours/day

**NE-IFOS-CARBO-ETOP****Ifosfamide-Carboplatin-
Etoposide (ICE)
Chemotherapy****ADVANCED LEVEL REGIMEN-
Provincial Cancer Centre***(Adjuvant Treatment of Glioma, Oligodendroglioma)***PREHYDRATION Day 1**

- May give Normal Saline 1000mL infuse over 1 hour

ETOPOSIDE 100 mg/m² IV Days 1 to 3 (Round to nearest 10mg)

- Premixed in 500mL bags of Normal Saline, connect piggyback to IV line. Infuse over 60 minutes. Adjust rate if blood pressure drops

CARBOPLATIN AUC= 5 mg/mL/min IV Day 1 (Round to nearest 5mg)

- Mix in 250mL bag (5% Dextrose). Infuse over 30 minutes

MESNA 600mg/m² IV Day 1 immediately before Ifosfamide

- Dilute in 50mL minibag (Normal Saline). Infuse over 15 minutes

IFOSFAMIDE 5000 mg/m² CIV Day 1 (Round to nearest 100mg. Usually given in hospital)

- Dilute in 2000mL Normal Saline (split dose into 2 x 1000mL bags to infused sequentially). Infuse over 24 hours

- May give concurrent hydration with 1-3L of IV fluid during infusion, to maintain high urine flow

MESNA 5000 mg/m² CIV Day 1

- Dilute in 2000mL Normal Saline- Admix in same bag as Ifosfamide; Infuse over 24 hours concurrent with Ifosfamide

MESNA 2500 mg/m² CIV Day 2

- Dilute in 2 x 1000mL bags (Normal Saline). Infuse over 12 hours immediately following Ifosfamide infusion

POSTHYDRATION

- May give Normal Saline 1000mL infuse over 1 hour concurrent with or following Mesna infusion

REPEAT EVERY 21 DAYSPHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**NOTE**Calvert AUC Dosing Formula

DOSE (mg)=target AUC x (GFR + 25)

- GFR expressed as measured Creatinine clearance (mL/min) or estimated from serum Creatinine

$$Cl_{Cr} \text{ (mL/sec)} = \frac{140 - \text{age (yr)}}{72} \times \frac{\text{TBW (kg)}}{Cr_{\text{serum}} \text{ (}\mu\text{mol/L)}}$$

$$Cl_{Cr} \text{ (mL/sec)} = Cl_{Cr} \text{ (mL/sec)} \times 0.85$$

NE

NE-IFOS-CARBO-ETOP

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO prechemo each day (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV- pre-chemo & 8mg PO qhs on Days 1 to 3 OR
 - Granisetron 2mg PO or 1mg IV prechemo each day, OR Dolasetron 100mg PO or 100mg IV prechemo each day). **AND**
- Dexamethasone 8mg PO prechemo each day (may increase to 20mg PO or IV)- *OMIT Dexamethasone if patient is already taking ≥ 16 mg per day.* **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO) *"When available in Canada"*

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses- *OMIT Dexamethasone if patient is already taking ≥ 16 mg per day.* **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) OR
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo. **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *"When available in Canada"*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

DOSE MODIFICATION

Urologic Toxicities

1. If RBC/HPF > 10, notify physician. **HOLD** Ifosfamide and continue Mesna

Hematologic Toxicities

1. If ANC < $1.5 \times 10^9/L$, or if Platelets < $100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Renal failure (Recommended action)

1. If Serum Creatinine = $136-150 \mu\text{mol/L}$ or Creatinine Clearance = $40-60 \text{ mL/min}$, **reduce** Carboplatin dose by **1 mg/mL/min** (or by **50 mg/m^2**)
2. If Serum Creatinine = $151-180 \mu\text{mol/L}$ or Creatinine Clearance = $20-40 \text{ mL/min}$, **reduce** Carboplatin dose by **2 mg/mL/min** (or by **100 mg/m^2**)
3. If Serum Creatinine > $181 \mu\text{mol/L}$ or Creatinine Clearance < 20 mL/min , **OMIT** Carboplatin dose & **reduce** Ifosfamide to 75% dose
4. If CrCl < 12 mL/min , **reduce** Ifosfamide & Etoposide to 50% dose

Hepatic dysfunction (Suggested action)

1. If Bilirubin = $26-51 \mu\text{mol/L}$ or AST = $60-180 \text{ IU/L}$ **reduce** Ifosfamide to 75% dose & Etoposide to 50% dose
2. If Bilirubin = $52-85 \mu\text{mol/L}$, **reduce** Ifosfamide to 50% dose & Etoposide to 25% dose

Continued Next Page

NE-IFOS-CARBO-ETOP

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes before each cycle of treatment
- Urinalysis (for RBCs/HPF) before each cycle of treatment
- Baseline & periodic hepatic function tests [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels]
- Baseline & periodic renal function tests [serum creatinine, serum electrolytes & BUN]
- Neurologic toxicity ratings (Sensory, Cortical) at each visit
- Baseline and periodic renal function tests [serum creatinine, electrolytes & BUN]; serum creatinine level before each cycle of chemotherapy
- Clinical assessment of stomatitis: oral examination upon patient complaint of a sore mouth
- Baseline blood pressure at each treatment; monitor for hypotension

SENSORY

- 0 No change
- 1 Mild paraesthesia, no deep tendon reflex
- 2 Mild/moderate sensory loss/moderate paraesthesia
- 3 Sensory loss interferes with function

CYSTITIS

- 0 None
- 1 Mild symptoms
- 2 Symptoms relieved with therapy
- 3 Symptoms not relieved
- 4 Life-threatening

CORTICAL

- 1 None
- 2 Mild somnolence
- 3 Moderate somnolence
- 4 Severe somnolence, confusion, hallucination
- 5 Coma, seizure

Rated at each clinic visit

PATIENT VISIT

CHEMOTHERAPY VISIT:

Approx. 2 hours/day

NE

NE-L-CARBO-V

Lomustine-Carboplatin- Vincristine Chemotherapy

(Glioma, Oligodendroglioma)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

LOMUSTINE 75 mg/m² PO Day 1

(Outpatient prescription in multiples of 10, 40 & 100mg capsules)

CARBOPLATIN AUC= 5 mg/mL/min IV Day 1 (Round to nearest 5mg)

- Mix in 250mL bag (5% Dextrose); Infuse over 30 minutes

POSTHYDRATION

- 500mL Normal Saline (may add 10mEq PotassiumChloride & 8 mmol Magnesium Sulfate); Infuse over 1 hour (increase fluids if poor oral intake)

VINCRIStINE 2 mg IV Days 1, 8 & 15 (Flat dose)

- Push through sidearm of free flowing IV; Inject over at least 1 minute

REPEAT EVERY 42 DAYS

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < $1.5 \times 10^9/L$ OR if Platelets < $100 \times 10^9/L$ on Day 1, notify physician and **HOLD** dose for 1 week (until ANC $\geq 1.5 \times 10^9/L$ & Platelets $\geq 100 \times 10^9/L$)
2. If ANC < $1.0 \times 10^9/L$ OR if Platelets < $75 \times 10^9/L$ on Days 8 or 15, notify physician and **HOLD** dose for 1 week

Renal failure (Recommended action)

1. If Serum Creatinine=136-150µmol/L or Creatinine Clearance =40-60mL/min, **reduce** Carboplatin dose by **1mg/mL/min** (or by **50mg/m²** for BSA dosing)
2. If Serum Creatinine=151-180µmol/L or Creatinine Clearance =20-40mL/min, **reduce** Carboplatin dose by **2mg/mL/min** (or by **100mg/m²** for BSA dosing)
3. If Serum Creatinine >181µmol/L, **DISCONTINUE** Carboplatin dose
4. If CrCl < 10mL/min, reduce Lomustine to **25-50%** dose

Hepatic dysfunction (Suggested action)

1. If Bili=26-51µmol/L or AST=60-180IU/L, reduce Vincristine to **50%** dose
2. If Bili= 52-85µmol/L, reduce Vincristine to **25%** dose

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

NOTE

Calvert AUC Dosing Formula

DOSE (mg)=target AUC x (GFR + 25)

• GFR expressed as measured Creatinine clearance (mL/min) or estimated from serum Creatinine Creatinine Clearance (X60 for mL/min)

$$Cl_{cr} \text{ ♂ } = \frac{140 - \text{age (yrs)}}{72} \times \frac{\text{TBW (kg)}}{Cr_{serum} (\mu\text{mol/L})}$$

$$Cl_{cr} \text{ ♀ } (\text{mL/sec}) = Cl_{cr} \text{ ♂ } \times 0.85$$

NE-L-CARBO-V

SUPPORTIVE CARE

ANTIEMETIC REGIMENS: Day 1- HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO prechemo (Ondansetron 8mg IV- prechemo) **OR**
 - Granisetron 2mg PO or 1mg IV prechemo each day, **OR** Dolasetron 100mg PO or 100mg IV prechemo each day). **AND**
 - Dexamethasone 20mg IV- *OMIT Dexamethasone if patient is already taking ≥ 16 mg per day.* **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO) *"When available in Canada"*

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses- *OMIT Dexamethasone if patient is already taking ≥ 16 mg per day.* **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo. **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *"When available in Canada"*

Days 8 & 15- LOW RISK

- Prochlorperazine 10mg PO (and/or PR) q4-6h PRN, or Metoclopramide 10mgPO q3-4h PRN

NOTE: *If vomiting not controlled, escalate antiemetic treatment (use Ondansetron, Granisetron or Dolasetron PO)- Vomiting may increase Intracranial Pressure with larger brain tumours*

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

NE

NE-L-CARBO-V

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Baseline and routine renal function tests [serum creatinine, electrolytes & BUN] and liver function tests [AST/ALT, Bilirubin]
- Periodic clinical pulmonary exam, incl. auscultation, pulmonary toxicity ratings (Cough, SOB)- if treatment for >6mo
- Neurologic toxicity ratings (Sensory) at each visit
- Baseline & periodic Hearing ratings, hearing tests if symptomatic

COUGH

- 0 None
- 1 Mild
- 2 Moderate
- 3 Severe

SHORT OF BREATH

- 0 No change
- 1 Abnormal PFT's
- 2 Dyspnea on exertion
- 3 Dyspnea at normal level of activity
- 4 Dyspnea at rest

Rated at each clinic visit every 2-3 months

CORTICAL

- 1 None
- 2 Mild somnolence
- 3 Moderate somnolence
- 4 Severe somnolence, confusion, hallucination
- 5 Coma, seizures

Rated at each clinic visit

PATIENT VISIT

CHEMOTHERAPY VISIT

Day 1: Chemotherapy Visit - Approx. 1-2 hours

Days 8 & 15: Chemotherapy Visit - Approx. 30 minutes

NE-LCV

Lomustine-Cisplatin- Vincristine Chemotherapy (Glioma, Oligodendroglioma)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

PREHYDRATION- Day 1

- Encourage patient to drink 6-8 glasses of water prior to chemo each day
- Prehydrate with 500mL Normal Saline; Infuse over 1 hour

CISPLATIN 75mg/m² IV Day 1 (Round to nearest 1mg)

- Mix drug in 500mL bag (Normal Saline); Infuse over 60 minutes;
- May also give 200mL of 10% Mannitol solution (20G); infuse through sidearm concurrent with Cisplatin (if diuresis needed)

POSTHYDRATION

- 500mL Normal Saline (may add 10mEq PotassiumChloride & 8 mmol Magnesium Sulfate); Infuse over 1 hour (increase fluids if poor oral intake)

LOMUSTINE 75mg/m² PO Day 1

(Outpatient prescription in multiples of 10, 40 & 100mg capsules)

VINCRIPTINE 2mg IV Days 1, 8 & 15 (Flat dose)

- Push through sidearm of free flowing IV; Inject over at least 1 minute

REPEAT EVERY 42 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMENS: Day 1- HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist IV (Ondansetron 8mg IV, OR Granisetron 1mg IV; OR Dolasetron 100mg IV). **AND**
- Dexamethasone 20mg IV (*eliminate if > 16mg Dexamethasone already in use*). **AND**
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO) *"When available in Canada"*

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses (*eliminate Dexamethasone if steroids already in use*). **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo. **AND**
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *"When available in Canada"*

Days 8 & 15- LOW RISK

- Prochlorperazine 10mg PO (and/or PR) q4-6h PRN, or Metoclopramide 10mgPO q3-4h PRN

NOTE: If vomiting not controlled, escalate antiemetic treatment (use Ondansetron, Granisetron or Dolasetron PO)- Vomiting may increase Intracranial Pressure with larger brain tumours

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

Continued Next Page...

NE-LCV

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Baseline and routine renal function tests [serum creatinine, electrolytes & BUN] and liver function tests [AST/ALT, Bilirubin]
- Periodic clinical pulmonary exam, incl. auscultation, pulmonary toxicity ratings (Cough, SOB)- if treatment for >6mo
- Neurologic toxicity ratings (Sensory) at each visit
- Baseline & periodic Hearing ratings; hearing tests if symptomatic

COUGH

0. None

1. Mild

2. Moderate

3. Severe

HEARING

0. No change

1. Asymptomatic

2. Tinnitus

3. Correctable hearing loss

4. Deafness

SHORT OF BREATH

0. No change

1. Abnormal PFT's

2. Dyspnea on exertion

3. Dyspnea at normal level of activity

4. Dyspnea at rest

Rated at each clinic visit every 2-3 months

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < $1.5 \times 10^9/L$ OR if Platelets < $100 \times 10^9/L$ on Day 1, notify physician and **HOLD** dose for 1 week (until ANC $\geq 1.5 \times 10^9/L$)
2. If ANC < $1.0 \times 10^9/L$ OR if Platelets < $75 \times 10^9/L$ on Days 8 or 15, notify physician and **HOLD** dose for 1 week

Renal failure (Recommended action)

1. If CrCl = 30-60mL/min or Serum Creatinine = 136-185 $\mu\text{mol/L}$; reduce to **50%** dose
2. If CrCl < 30mL/min or Serum Creatinine > 185 $\mu\text{mol/L}$; **Omit** dose
3. If CrCl < 10mL/min, reduce Lomustine to **25-50%** dose

Hepatic dysfunction (Suggested action)

1. If Bili = 26-51 $\mu\text{mol/L}$ or AST = 60-180 IU/L, reduce Cisplatin & Vincristine to **50%** dose
2. If Bili = 52-85 $\mu\text{mol/L}$, reduce Cisplatin & Vincristine to **25%** dose
3. If Bili > 85 $\mu\text{mol/L}$ or AST > 180 IU/L, **Omit** dose

NOTE

Calvert AUC Dosing Formula

DOSE (mg) = target AUC x (GFR + 25)

• GFR expressed as measured

Creatinine clearance (mL/min) or

estimated from serum Creatinine

Creatinine Clearance (X60 for mL/min)

$Cl_{Cr} \text{ } \sigma = \frac{140 - \text{age (yrs)} \times \text{TBW (kg)}}{50 \times Cr_{\text{Serum}} (\mu\text{mol/L})}$

(mL/sec)

$Cl_{Cr} \text{ } \phi (\text{mL/sec}) = Cl_{Cr} \text{ } \sigma \times 0.85$

PATIENT VISIT

CHEMOTHERAPY VISIT:

Day 1: Chemotherapy Visit: - Approx. 4-5 hours

Days 8 & 15: Chemotherapy Visit: - Approx. 30

NE-LOMUST

Lomustine Chemotherapy

(Glioma, Oligodendroglioma-Adjuvant Treatment)

**Take-Home Prescription-
Special Authorization Required**

LOMUSTINE 130mg/m² PO Day 1

(Outpatient prescription in multiples of 10, 40 & 100mg capsules)

REPEAT EVERY 42 DAYS For a Usual Total of 6 to 7 Cycles

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy:

- Serotonin Receptor Antagonist PO/ IV (i.e. Ondansetron 8-16mg PO or 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), and
- Dexamethasone 20mg IV (*eliminate Dexamethasone if steroids already in use*)

Post-Chemotherapy:

- Dexamethasone 8 mg PO twice daily for 2 to 3 days (*eliminate Dexamethasone if steroids already in use*), and
- Metoclopramide 10-40 mg PO two to four times per day for 2-3 days, or a Serotonin Receptor Antagonist PO (i.e. Ondansetron 8mg PO q12h for 2-3 days, or Granisetron 2mg PO q24h for 2-3 days, or Dolasetron 100mg PO q24h for 2-3 days)
- If vomiting not controlled during first treatment cycle, substitute for alternate setron antiemetic (use Dolasetron or Granisetron PO) or escalate antiemetic treatment doses- Vomiting may increase Intracranial Pressure with larger brain tumours

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.0 x 10⁹/L OR if Platelets < 75 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Renal failure (*Suggested action*)

1. If CrCl < 10mL/min, reduce Lomustine to **25-50%** dose

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Periodic **clinical pulmonary exam**, incl auscultation, pulmonary toxicity ratings (Cough, SOB)- if treatment for >6mo
- Baseline **renal function tests** (if failure suspected) [serum creatinine, electrolytes & BUN]

SHORT OF BREATH

0. No change
1. Abnormal PFT's
2. Dyspnea on exertion
3. Dyspnea at normal level of activity
4. Dyspnea at rest

COUGH

0. None
1. Mild
2. Moderate
3. Severe

Rated at each clinic visit every 2-3 months

NE

NE-PLV

Procarbazine-Lomustine-Vincristine (PCV) Chemotherapy

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

(Adjuvant Treatment of Glioma, Oligodendroglioma)

LOMUSTINE 110mg/m² PO Day 1

(Outpatient prescription in multiples of 10, 40 & 100mg capsules)

VINCRIPTINE 1.4mg/m² IV Day 8 & Day 29

(Round to nearest 0.1mg - to a maximum dose of 2mg)

- Push through sidearm of free flowing IV; Inject over at least 1 minute

PROCARBAZINE 60mg/m² PO Days 8 to 21

(Outpatient prescription in multiples of 50mg capsules)

REPEAT EVERY 42 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMENS: Day 1- HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO, OR Granisetron 2mg PO, OR Dolasetron 100mg PO)

Post-Chemotherapy-

- If vomiting not controlled during treatment, escalate antiemetic treatment- Vomiting may increase Intracranial Pressure with larger brain tumours
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo. **AND**
 - Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses, OR Granisetron 2mg PO q24h for 2 doses, OR Dolasetron 100mg POq24h for 2 doses)

Days 8 to 21- **INTERMEDIATE RISK**

- Serotonin Receptor Antagonist before each Procarbazine dose (Ondansetron 8mg PO, OR Granisetron 2mg PO, OR Dolasetron 100mg PO)

OTHER SUPPORTIVE CARE

- Diet with low tyramine content and no alcoholic beverages during Procarbazine days

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

NE-PLV

CLINICAL MONITORING

- **Complete blood count including differential, platelets and hemoglobin (CBC)** before each cycle of treatment
- **Periodic clinical pulmonary exam**, incl. auscultation, pulmonary toxicity ratings (Cough, SOB)- if treatment for >6mo
- **Renal function tests** [serum creatinine, electrolytes & BUN], **liver function tests** [AST/ALT, Bilirubin] and **serum glucose** checked before chemo on Day 1 of each cycle

SHORT OF BREATH

- 0 No change
- 1 Abnormal PFT's
- 2 Dyspnea on exertion
- 3 Dyspnea at normal level of activity
- 4 Dyspnea at rest

COUGH

- 0 None
- 1 Mild
- 2 Moderate
- 3 Severe

Rated at each clinic visit every 2-3 months

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < $1.5 \times 10^9/L$ OR if Platelets < $100 \times 10^9/L$ on Days 1 or 8, notify physician and **HOLD** dose for 1 week (until ANC $\geq 1.5 \times 10^9/L$)
2. If ANC < $1.0 \times 10^9/L$ OR if Platelets < $75 \times 10^9/L$ on Day 29, notify physician and **HOLD** dose for 1 week

Renal failure

1. If CrCl < 10mL/min, reduce Lomustine to **25-50%** dose and consider dose reduction of Procarbazine (*Suggested action*)

Hepatic dysfunction

1. If Bili = 25-50 μ mol/L or AST = 60-180IU/L, reduce Vincristine to **50%** dose
2. If Bili >50 μ mol/L or AST > 180IU/L, reduce Vincristine to **25%** dose (*Suggested action*)

PATIENT VISIT

CHEMOTHERAPY VISIT:

Days 8 & 29-Approx. 30 minutes

NE

NE-TEMOZOL

Temozolomide Chemotherapy

**Take-Home Prescription-
Special Authorization Required**

(Glioblastoma Multiforme or Anaplastic Astrocytoma-
Palliative Treatment after Recurrence or Progression from Standard Therapy)

TEMOZOLOMIDE 150-200 mg/m² PO Days 1 to 5

Increase to 200mg/m² PO days 1-5 if no myelosuppression at Day 22 nadir
(Outpatient prescription in multiples of 5mg, 20mg, 100mg & 250mg capsules)

REPEAT EVERY 28 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: INTERMEDIATE RISK

- Ondansetron 8mg PO & Dexamethasone 8-20mg PO before each oral chemo dose, days 1 to 5 (*eliminate Dexamethasone if steroids already in use*)
- Ondansetron 8mg PO & Dexamethasone 8mg PO 12 hours after each oral dose & q12h for 2-3 days after last chemo treatment (total of 14-16 doses, at 12 hour intervals, from start)
- *If vomiting not controlled during first treatment cycle, substitute for alternate setron antiemetic (use Dolasetron or Granisetron PO) or escalate antiemetic treatment doses- Vomiting may increase Intracranial Pressure with larger brain tumours*

GUIDELINE

See the CCNS website
www.cancercare.ns.ca for the
guideline on Temozolomide for
malignant glioma

CLINICAL MONITORING

NO RECOMMENDED TOXICITY
RATINGS

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.0×10^9 /L or if Platelets < 50×10^9 /L during any cycle, the next cycle must be reduced

PHYSICIAN'S STANDING ORDERS AVAILABLE FOR THIS REGIMEN

NOTES

- Prescription costs covered by some third party prescription plans; for Pharmacare approval the prescriber must write a letter of request for each patient (Note: This indication is NOT covered in the guideline for Temozolomide, often used by Pharmacare to determine coverage)
- The cost per treatment course (i.e. 14 days) can range from \$1,000-1,500, depending upon patient size

REGIMEN CONTENTS

OC-CISP-ETOP - *Cisplatin-
Etoposide Chemotherapy*

OC-FU-LEUC - *LowDose 5-
Fluorouracil-Leucovorin*

OC-PACLI-CARB - *Paclitaxel-
Carboplatin Chemotherapy*

OC-PCE- *Paclitaxel-Carboplatin-
Etoposide Chemotherapy* 500

NOTE: *Regimen names in italics are
not in this pocketbook version- See
full version for regimen monograph*

**OC-PCE****Paclitaxel-Carboplatin-
Etoposide Chemotherapy**

(Occult Cancer- Adenocarcinoma of
Unknown Origin)

INTERMEDIATE LEVEL REGIMEN
Regional Hospital with Dedicated
Cancer Treatment Unit

PREMEDICATIONS:

DEXAMETHASONE 20mg PO 12 & 6 hours before Paclitaxel

OR- 20mg IV starting 45 minutes before Paclitaxel

DIPHENHYDRAMINE 50mg IV & RANITIDINE 50mg IV

- Admixed together in 50mL minibag of Normal Saline. Give over 15 minutes, starting 30 minutes before Paclitaxel

PACLITAXEL 225mg/m² IV Infuse over 3 hours Day 1

(Round to nearest 3mg)

- Mix in 500mL bag (5% Dextrose- dilution concentration 0.3-1.2 mg/mL). Use non-PVC equipment, including 0.22 micron in-line filter. Infuse over 3 hours
- Take a baseline blood pressure measurement, if prior hypotension

CARBOPLATIN AUC= 6 mg/mL/min IV Day 1 (Round to nearest 5mg)

- Mix in 250mL bag (5% Dextrose). Infuse over 30 minutes
- May infuse concurrently with Paclitaxel, using a Y-connector

ETOPOSIDE 50mg PO daily or **100mg** PO on alternate days daily for 10 days

(Retail prescription in 50mg capsules)

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE**ANTIEMETIC REGIMEN: INTERMEDIATE RISK**Pre-Chemotherapy-

- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO. OR Granisetron 2mg PO. OR Dolasetron 100mg PO)

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses. **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- May give a Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO/ 10mg PR q4h PRN post chemo **OR** Metoclopramide 10mg PO q4-6h PRN post chemo)

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

OC-PCE

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) and serum electrolytes (including Mg^{2+}) before each cycle of treatment
- Baseline and periodic renal function tests [serum creatinine, electrolytes & BUN], serum creatinine level before each cycle of chemotherapy
- Liver function tests [GGT, ALT, AST & Bilirubin levels] before each cycle of treatment
- Watch for symptoms of fever or infection
- Neurologic (Sensory), hypersensitivity and flu-like symptoms toxicity ratings at each visit
- Baseline blood pressure and pulse rate monitoring during drug administration & for the following hour

SENSORY

- 0 No change
- 1 Mild paraesthesia, no deep tendon reflex
- 2 Mild/moderate sensory loss, moderate paraesthesia
- 3 Sensory loss interferes with function

FLU-LIKE SYMPTOMS

(Arthralgia, myalgia)

- 0 None
- 1 Mild
- 2 Moderate
- 3 Severe

HYPERSENSITIVITY/ALLERGY

- 0 None
- 1 Transient rash, fever $<38^{\circ}\text{C}$
- 2 Urticaria, fever $\geq 38^{\circ}\text{C}$, mild bronchospasm
- 3 Serum sickness, bronchospasm, requires parenteral meds
- 4 Anaphylaxis

Rated at each clinic visit

DOSE MODIFICATION

Hematologic Toxicities

- 1 If ANC $< 1.5 \times 10^9/\text{L}$, or if Platelets $< 100 \times 10^9/\text{L}$, notify physician and HOLD dose for 1 week

Hepatic dysfunction (Suggested action)

- 1 If Bilirubin $\geq 25\mu\text{mol/L}$, give Paclitaxel maximum dose of $135\text{mg}/\text{m}^2$
- 2 If Bilirubin = $26-51\mu\text{mol/L}$ or AST = $60-180\text{IU/L}$, give Paclitaxel maximum dose of $75\text{mg}/\text{m}^2$
- 3 If Bilirubin = $52-85\mu\text{mol/L}$, give Paclitaxel maximum dose of $50\text{mg}/\text{m}^2$

Renal failure (Recommended action)

- 1 If Serum Creatinine = $136-150\mu\text{mol/L}$ or Creatinine Clearance = $40-60\text{mL}/\text{min}$, reduce Carboplatin dose by $1\text{mg}/\text{mL}/\text{min}$ (or by $50\text{mg}/\text{m}^2$ for BSA dosing)
- 2 If Serum Creatinine = $151-180\mu\text{mol/L}$ or Creatinine Clearance = $20-40\text{mL}/\text{min}$, reduce Carboplatin dose by $2\text{mg}/\text{mL}/\text{min}$ (or by $100\text{mg}/\text{m}^2$ for BSA dosing)
- 3 If Serum Creatinine $> 181\mu\text{mol/L}$ or Creatinine Clearance $< 20\text{mL}/\text{min}$, OMIT Carboplatin dose

OC-PCE

NOTE

Calvert AUC Dosing Formula

DOSE (mg)=target AUC x (GFR + 25)

• GFR expressed as measured Creatinine clearance (mL/min) or estimated from serum Creatinine Creatinine Clearance (X60 for mL/min)

$$Cl_{\text{Cr}} \text{ (mL/sec)} = \frac{140 - \text{age (yr)}}{72} \times \frac{\text{TBW (kg)}}{Cr_{\text{serum}} \text{ (mg/dL)}}$$

$$Cl_{\text{Cr}} \text{ (mL/sec)} = Cl_{\text{Cr}} \text{ (mL/sec)} \times 0.85$$

PATIENT VISIT

CHEMOTHERAPY VISIT

Approx. 5 hours OR- Approx 4 1/2 hours if concurrent

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505

PR-DOCETAX - Docetaxel
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Chemotherapy 505

PR-ESTRA-VINB - Estramustine-
Vinblastine Chemotherapy

PR-FLUT - Flutamide Therapy 508

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509

PR-MITOX-PRED - Mitoxantrone-
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PR-MEGES - Megestrol Therapy

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NOTE

Hormone combinations for complete androgen blockade are NOT listed as separate regimens. Combinations usually include an antitestosterone agent (PR-BICAL, PR-FLUT, PR-NILUT) with an LHRH antagonist (PR-BUSER, PR-GOSE, PR-LEUPRO). These combinations may be used prior to surgery (orchiectomy) or in place of surgery. Please refer to treatment guidelines for prostate cancer (Genitourinary Cancer Site Team) for further information on hormone combinations.

NOTE: Regimen names in italics are not in this pocketbook version. See full version for regimen monograph.

PR-BICAL

Bicalutamide (Casodex) Therapy

Take-Home Prescription- Unrestricted

(Prostate Cancer (Locally Advanced- Stage C)- Neoadjuvant Curative Intent
Prostate Cancer (Metastatic- Stage D)- Palliative Intent)

BICALUTAMIDE 50mg PO daily

(Outpatient prescription in multiples of 50mg tablets)

CONTINUOUS TREATMENT

DOSE MODIFICATION

Hepatic failure (Suggested action)

If AST or ALT > 105IU/L, **STOP**
treatment

NOTE

- Prescription costs covered by all third party prescription plans

CLINICAL MONITORING

- Periodic **liver function tests**
(serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated)

[Rev 11/01]

PR-BUSER

Buserelin Therapy

Take-Home Prescription- Physician Office Administration

(Prostate Cancer (Locally Advanced- Stage C)- Neoadjuvant Curative Intent
Prostate Cancer (Metastatic- Stage D)- Palliative Intent)

BUSERILIN 6.3mg SC DEPOT Day 1

(Fixed-dose injection kits of 6.3mg in 2 depot implant rods, given as a single injection)

- Subcutaneous injection of depot in hospital, Cancer Centre or physician's office; drug supplied by retail prescription

CONTINUOUS TREATMENT REPEAT EVERY 56 DAYS

NOTES

- Prescription costs covered by all third party prescription plans
- May give initial treatment with daily SC injections of 500µg TID for 7 days (Buserelin Injection), and an antiandrogen medication (Bicalutamide/ Flutamide/Nilutamide) started 4 weeks prior to the initiation of Buserelin
- Patient may prefer maintenance therapy with Buserelin Nasal Solution; equivalent dosing is 400µg (2 measured 100µg doses per nostril) TID

[Rev 11/01]

PR-CYPROT

Cyproterone Therapy

(Prostate Cancer (Metastatic-
Stage D)- Palliative Intent)

Take-Home Prescription-
Unrestricted

CYPROTERONE 50-100mg PO BID or TID

(Outpatient prescription in multiples of 50mg tablets)

CONTINUOUS TREATMENT

CLINICAL MONITORING

- Baseline & periodic **liver function tests** (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated)

NOTE

- Prescription costs covered by all third party prescription plans

[Rev 11/01]

PR-ESTRAMUST

Estramustine Chemotherapy

(Hormone-Resistant Prostate Cancer)

Take-Home Prescription-
Unrestricted

ESTRAMUSTINE 280mg PO BID

(up to 8 or 9 capsules daily, as tolerated or 14mg/Kg/d round to the nearest capsule)

(Outpatient prescription in multiples of 140mg tablets)

CONTINUOUS TREATMENT Until disease progression

SUPPORTIVE CARE

ANTIEMETIC REGIMEN NOT
APPLICABLE

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Baseline and periodic liver function tests (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels) and blood pressure measurement

NOTE

This regimen should only be used for hormone-resistant prostate cancer, in patients who can tolerate cytotoxic therapy.

PR

[Rev 11/01]

PR-DOCE-PRED

Docetaxel Chemotherapy

(Hormone-Resistant Prostate Cancer)

INTERMEDIATE LEVEL REGIMEN-

Regional Hospital with Dedicated
Cancer Treatment Unit

PREMEDICATIONS:

DEXAMETHASONE 8mg PO, 3 doses before chemotherapy (evening before, morning of and 1 hour before chemotherapy), then 8mg PO BID for 3 doses after chemotherapy

DOCETAXEL 75 mg/m² IV Day 1 (Round to nearest 3mg)

- Mix in 250mL bag (5% Dextrose or Normal Saline) to a maximum concentration of 1.0-0.3mg/mL; Use non-PVC tubing; Infuse through main IV line over 1 hour

PREDNISONE 5mg PO BID

(Outpatient prescription in multiples of 5mg tablets)

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

INTERMEDIATE RISK

Pre-Chemotherapy-

- Dopamine Receptor Antagonist PO (Prochlorperazine 10mg PO, or Metoclopramide 10mg PO)

Post-Chemotherapy-

- Dopamine Receptor Antagonist PRN ((Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10mg PO q4h PRN)

DEXAMETHASONE Alternate Pre- & Postmedication Regimens:

- May give 20mg PO 12hr & 6hr before chemotherapy, then 8mg PO bid for 4 days after chemotherapy
- May give 8mg PO at 13hr, 7hr & 1hr before chemotherapy, then 8mg PO bid for 3 days after chemotherapy

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

DOSE MODIFICATION

Hematologic Toxicities

- 1 If ANC < 1.5 x 10⁹/L or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Hepatic dysfunction

- 1 If AST or ALT > 60IU/L (>1.5X ULN) or if Alk Phos > 300IU/L (>2.5X ULN), reduce Docetaxel to **75% dose**
- 2 If AST or ALT > 200IU/L (>5X ULN) or if Alk Phos > 600IU/L (>5X ULN) **HOLD** Docetaxel dose and contact physician

ALTERNATE ADJUSTMENT

- 3 If LFTs > 1.5x ULN or Bilirubin > ULN (>26μmol/L) during treatment **HOLD** Docetaxel dose for 3 weeks and re-test
ULN = upper limit of normal for lab value
(Recommended action)

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

Continued Next Page...

PR-DOCE-PRED

CLINICAL MONITORING

- **Complete blood count** including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- **Baseline liver function tests** (if liver failure suspected) [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]
- Watch for symptoms of **fever or infection**
- **Clinical assessment of stomatitis**, oral examination upon patient complaint of a sore mouth
- **Skin assessment** at each visit, including nails and infusion veins
- Monitor **fluid retention** at each visit

SKIN TOXICITY

0. None
1. Hyperpigmentation
2. Atrophy
3. Subcutaneous fibrosis
4. Desquamation, ulceration, or necrosis

NAIL CHANGES

0. Normal
1. Discolouration or ridging (Vailonychia) or pitting
2. Partial or complete loss of nail(s) or pain in nailbeds
3. -
4. -

FLUID RETENTION

0. None
1. Mild peripheral edema
2. Pleural edema, outpatient management
3. Pleural edema, inpatient management
4. Intubation required

Rated at each clinic visit

GUIDELINE

See the CCNS website www.cancercare.ns.ca for the guideline on Docetaxel for hormone-resistant prostate cancer

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:
Approximately 2 hours

PR-FLUT

Flutamide Therapy

Take-Home Prescription- Unrestricted

(Prostate Cancer (Locally Advanced- Stage C)- Neoadjuvant Curative Intent
Prostate Cancer (Metastatic- Stage D)- Palliative Intent)

FLUTAMIDE 250mg PO TID (Outpatient prescription in multiples of 250mg tablets)

CONTINUOUS TREATMENT

DOSE MODIFICATION

Hepatic failure (Suggested action)
If AST or ALT > 105IU/L, **STOP**
treatment

NOTE

- Prescription costs covered by all third party prescription plans

CLINICAL MONITORING

- Periodic **liver function tests** (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated)

[Rev 11/01]

PR-GOSER

Goserelin Therapy

Take-Home Prescription- Physician Office Administration

(Prostate Cancer (Locally Advanced- Stage C)- Neoadjuvant Curative Intent
Prostate Cancer (Metastatic- Stage D)- Palliative Intent)

GOSERILIN 3.6mg SC DEPOT q28d OR 10.8mg SC DEPOT Day 1
(Fixed-dose injection kits of 3.6mg or 10.8mg depot pellet)

- Subcutaneous injection of depot in hospital, Cancer Centre or physician's office;
drug supplied by retail prescription

CONTINUOUS TREATMENT

REPEAT EVERY 28 DAYS (3.6mg) OR 84 DAYS (10.8mg)

NOTES

- Prescription costs covered by all third party prescription plans

CLINICAL MONITORING

- Periodic **liver function tests** (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated)

[Rev 11/01]

PR-LEUPRO

Leuprolide Therapy

Take-Home Prescription-
Physician Office Administration

(Prostate Cancer (Locally Advanced - Stage C) - Neoadjuvant Curative Intent
Prostate Cancer (Metastatic- Stage D)- Palliative Intent)

LEUPROLIDE 7.5mg IM DEPOT OR 22.5mg IM DEPOT Day 1

(Fixed-dose injection kits of 7.5mg or 22.5mg depot)

- Intramuscular injection in hospital, Cancer Centre or physician's office; drug supplied by retail prescription

CONTINUOUS TREATMENT

REPEAT EVERY 28 DAYS (7.5mg) OR 84 DAYS (22.5mg)

NOTE

- Prescription costs covered by all third party prescription plans

[Rev 11/01]

PR-NILUT

Nilutamide Therapy

Take-Home Prescription-
Unrestricted

(Prostate Cancer (Locally Advanced- Stage C)-Neoadjuvant Curative Intent
Prostate Cancer (Metastatic- Stage D)- Palliative Intent)

NILUTAMIDE 100-150mg PO DAILY (50mg BID-TID)

(Outpatient prescription in multiples of 50mg tablets)

CONTINUOUS TREATMENT

DOSE MODIFICATION

Hepatic failure (Suggested action)

If AST or ALT > 105IU/L, **STOP**
treatment

CLINICAL MONITORING

- Periodic liver function tests
(serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated)

NOTE

Prescription costs covered by all third party prescription plans

PR

[Rev 11/01]

PR-MITOX-PRED

Mitoxantrone-Prednisone

Chemotherapy

(Hormone-Resistant Prostate Cancer)

INTERMEDIATE LEVEL REGIMEN-

Regional Hospital with Dedicated
Cancer Treatment Unit

MITOXANTRONE 12mg/m² IV Day 1 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV

PREDNISONE 5mg PO BID (Outpatient prescription in multiples of 5mg tablets)

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: INTERMEDIATE RISK

Pre-Chemotherapy-

- Dopamine Receptor Antagonist PO
(Prochlorperazine 10mg PO or
Metoclopramide 10-20mg PO)

Post-Chemotherapy-

- Prochlorperazine 10mg PO q4-6h
PRN, or Metoclopramide 10mg PO
q3-4h PRN

DOSE MODIFICATION

Hematologic Toxicities:

1. If WBC < 3.0 x 10⁹/L, notify
physician and **HOLD** dose for 1
week
2. If Platelets < 100 x 10⁹/L, notify
physician and **HOLD** dose for 1
week

Hepatic dysfunction

1. If Bili > 50µmol/L or AST > 180IU/L,
reduce Mitoxantrone to **50%** dose

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

Continued Next Page...

PR-MITOX-PRED

SUPPORTIVE CARE

- **Complete blood count** including differential, platelets, electrolytes and hemoglobin (CBC) and **serum uric acid levels** before each cycle of treatment
- Clinical exam for symptoms of **Congestive Heart Failure**
- Periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels
- Baseline **liver function tests** (especially if poor Performance Status) (serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated)
- **Serum glucose levels** (monitor routinely for diabetic patients)

CARDIAC At cumulative dose threshold

0. None and subsequent intervals

1. —
2. Asymptomatic, resting ejection fraction decline by >10% baseline, or abnormal cardiac function tests (LVEF >50) with no baseline for comparison
3. Mild Congestive Heart Failure, responds to therapy
4. Severe/refractory Congestive Heart Failure

At cumulative dose threshold and subsequent intervals

For Cardiac Toxicity Ratings:

First rating at the cumulative dose **threshold of 150mg/m²**, & repeat ratings at each cumulative dose **increment of 50mg/m²** above threshold (Cumulative dose sooner for high risk patients, eg pre-existing cardiac disease, prior chest irradiation)

Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given; cardiotoxicity is additive.

PATIENT VISIT

CHEMOTHERAPY VISIT

Approximately 30 minutes

PR

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NOTE

Regimens listed for common types of Sarcoma:

Ewing's Sarcoma- SA-CVD, SA-CVD-IE, SA-IFOS-ETOP

Kaposi's Sarcoma- SA-IFM*KAP, SA-VINBLAST, SA-VINCRIST

Osteosarcoma- SA-CISP-DOXO, SA-IFOS-ETOP

Soft Tissue Sarcoma- SA-DOXORUB, SA-IFOS-1D, SA-IFOS-5D, SA-IFOS-W

NOTE: *Regimen names in italics are not in this pocketbook version- See full version for regimen monograph*

SA-CVD

**Vincristine-Doxorubicin-
Cyclophosphamide (VAC)**

(Ewing's Sarcoma, Osteogenic
Sarcoma)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

PREHYDRATION

- Encourage patient to drink 6-8 glasses of water prior to chemo each day
- May give 1000mL Normal Saline; Infuse over 1 hour before chemotherapy

VINCRIStINE 1.4mg/m² IV Day 1

- Push through sidearm of free flowing IV; Inject over at least 1 minute

DOXORUBICIN 75mg/m² IV Day 1

- Slow push through sidearm of free flowing IV over at least 3-5 minutes
(Round to nearest 1mg)

CYCLOPHOSPHAMIDE 1200mg/m² IV Day 1 (Round to nearest 10mg)

- Mix in 500mL bag (5% Dextrose, Normal Saline); Infuse over 2 hours

MESNA 500mg/m² IV after Cyclophosphamide Day 1

- Dilute in 50mL bag (Normal Saline); Infuse over 15 minutes

POSTHYDRATION

- May give Normal Saline 1000mL infuse over 1 hour

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), **AND**
- Dexamethasone 8mg PO or IV

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)
- Oral hydration is strongly encouraged, poorly hydrated patients may need more IV hydration
- Inadequate total hydration may result in dose-related hemorrhagic cystitis

**PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN**

PATIENT VISIT
CHEMOTHERAPY VISIT:
Approximately 2 hours

SA

SA-CVD

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Baseline **hepatic function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated] and **renal function tests** (if failure suspected) [serum creatinine, serum electrolytes & BUN], before each cycle of treatment
- **Urinalysis** (for RBCs/HPF) before each cycle of treatment
- Clinical exam for symptoms of **Congestive Heart Failure**
- Baseline and periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels
- **Neurologic toxicity ratings** (Sensory, Constipation) at each visit

CONSTIPATION

0. No change
1. Mild
2. Moderate
3. Severe
4. Ileus >96 hours

SENSORY

0. No change
1. Mild paraesthesia, no deep tendon reflex
2. Mild/moderate sensory loss, moderate paraesthesia
3. Sensory loss interferes with function

Rated at each clinic visit

At cumulative dose threshold and subsequent intervals

CARDIAC

0. None
1. —
2. Asymptomatic, resting ejection fraction decline by >10% baseline, or abnormal cardiac function tests (LVEF >50) with no baseline for comparison
3. Mild Congestive Heart Failure, responds to therapy
4. Severe/refractory Congestive Heart Failure

For Cardiac Toxicity Ratings

First rating at the cumulative dose threshold of 300mg/m², & repeat ratings at each cumulative dose increment of 100mg/m² above threshold (Cumulative dose sooner for high risk patients, eg pre-existing cardiac disease, prior chest irradiation)

Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given, cardiotoxicity is additive

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets <100 x 10⁹/L, notify physician and **HOLD** dose for 1 week (Until ANC ≥ 1.5 x 10⁹/L)

Renal failure

1. If Serum Creatinine >265µmol/L, reduce Doxorubicin to **50%** dose
2. If CrCl < 12mL/min, **OMIT** Cyclophosphamide dose (*Suggested action*)

Hepatic dysfunction (*Suggested action*)

1. If Bilirubin=25-50µmol/L or AST =60-180IU/L, **reduce** Doxorubicin and Vincristine to **50%** dose
2. If Bilirubin= 51-85µmol/L or AST>180IU/L, reduce Cyclophosphamide to **75%** dose, & Doxorubicin and Vincristine to **25%** dose
3. If Bilirubin > 85µmol/L, **OMIT** ALL drugs

SA-CISP-DOXO

Cisplatin-Doxorubicin Chemotherapy

(Osteogenic Sarcoma)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

PREHYDRATION Day 1

- Encourage patient to drink 6-8 glasses of water prior to chemo each day
- 1000mL Normal Saline with 20mEq/L Potassium Chloride; Infuse over 1 hour

CISPLATIN 100mg/m² IV day 1 (Round to nearest 1mg)

- Split dose & mix in 4 x 1000mL bag (Normal Saline); Infuse 4000mL over 24 hours; may infuse 200mL Mannitol 10% concurrent with first 1000mL bag (Inpatient treatment)

DOXORUBICIN 25mg/m² IV days 1 to 3 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV over at least 3-5 minutes

POSTHYDRATION Day 2

- 1000mL Normal Saline; Infuse over 1 hour
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration

REPEAT EVERY 21 DAYS For a Usual Total of 6 Cycles

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy:

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), AND
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO) *"When available in Canada"*

Post-Chemotherapy:

- Dexamethasone 8 mg PO q24h for 3 doses. AND
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) OR
- No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo OR
- Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *"When available in Canada"*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)

OTHER SUPPORTIVE CARE

- If previous episode of febrile neutropenia, give Filgrastim 5µg/Kg SC daily following chemotherapy

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

PATIENT VISIT

CHEMOTHERAPY VISIT:

Day 1: Approx. 4 -6 hours)

Days 2&3: Approx. 45 minutes

Continued Next Page

SA-CISP-DOXO

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Serum creatinine and electrolytes
- Baseline and routine **renal function tests** [serum creatinine, serum albumin, serum electrolytes (including Mg^{++}) & BUN] before each treatment cycle and on Day 3 of each cycle
- Baseline and periodic **urine output and urinalysis tests** with high doses
- Clinical exam for symptoms of **Congestive Heart Failure**
- Baseline and periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels
- Baseline **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]

HEARING

- 0 No change
1. Asymptomatic
2. Tinnitus
3. Correctable hearing loss
4. Deafness

SENSORY

- 0 No change
1. Mild paraesthesia; no deep tendon reflex
2. Mild/moderate sensory loss, moderate paraesthesia
3. Sensory loss interferes with function

Rated at each clinic visit

CARDIAC

- 0 None
- 1 —
- 2 Asymptomatic, resting ejection fraction decline by $>10\%$ baseline, or abnormal cardiac function tests (LVEF >50) with no baseline for comparison
3. Mild Congestive Heart Failure, responds to therapy
- 4 Severe/refractory Congestive Heart Failure

For Cardiac Toxicity Ratings

First rating at the cumulative dose threshold of $300mg/m^2$, & repeat ratings at each cumulative dose increment of $100mg/m^2$ above threshold (Cumulative dose sooner for high risk patients, eg. pre-existing cardiac disease, prior chest irradiation)

Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given, cardiotoxicity is additive

DOSE MODIFICATION

Hematologic Toxicities

1. If $ANC < 1.5 \times 10^9/L$ OR if Platelets $< 100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Renal failure (Recommended action)

1. If $CrCl = 30-60mL/min$ or Serum Creatinine $= 136-185\mu mol/L$, **reduce** Cisplatin to 50% dose
2. If $CrCl < 30mL/min$ or Serum Creatinine $> 185\mu mol/L$, **Omit** Cisplatin dose

Hepatic dysfunction (Suggested action)

1. If $Bili = 26-51\mu mol/L$ or $AST = 60-180IU/L$, **reduce** Cisplatin and Doxorubicin to 50% dose
2. If $Bili = 52-85\mu mol/L$, **reduce** Cisplatin and Doxorubicin to 25% dose
3. If $Bili > 85\mu mol/L$ or $AST > 180IU/L$, **Omit** dose

[Rev 05/02]

SA-DOXORUB

Doxorubicin Chemotherapy

(Soft Tissue Sarcoma)

INTERMEDIATE LEVEL REGIMEN
Regional Hospital with Dedicated
Cancer Treatment Unit

DOXORUBICIN 75mg/m² IV Day 1 (Round to nearest 1mg)

- Slow push through sidearm of free flowing IV over at least 3-5 minutes
- Slow down injection rate if erythematous streaking occurs

REPEAT EVERY 21 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

INTERMEDIATE RISK

Pre-Chemotherapy:

- Serotonin Receptor Antagonist
(Ondansetron 8mg PO- may substitute
Ondansetron 8mg IV, or Granisetron
2mg PO or 1mg IV, or Dolasetron 100-
200mg PO or 100mg IV). **AND**
- Dexamethasone 8mg PO (may
increase to 20mg PO or IV)

Post-Chemotherapy:

- Dexamethasone 8 mg PO q24h for 3
doses. **AND**
- Serotonin Receptor Antagonist PO
(Ondansetron 8mg PO q12h for 3
doses if given prechemo) **OR**
- No post-chemo serotonin receptor
antagonist if Granisetron or
Dolasetron given pre-chemo **OR**
- Granisetron 2mg PO q24h for 1-2
days, or Dolasetron 100mg PO q24h
for 1-2 days if given pre-chemo

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets
< 100 x 10⁹/L, notify physician and
HOLD dose for 1 week

Renal failure

1. If Serum Creatinine > 265µmol/L,
reduce Doxorubicin to **50%** dose

Hepatic dysfunction

1. If Bilirubin = 26-51µmol/L or AST = 60-
180IU/L, give **50%** of Doxorubicin
dose
2. If Bilirubin = 52-85µmol/L or AST > 180IU/L,
give **25%** of Doxorubicin dose
3. If Bilirubin > 85µmol/L, **OMIT** Doxorubicin
dose
(Suggested action)

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

SA-DOXORUB

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Clinical exam for symptoms of **Congestive Heart Failure**
- Baseline and periodic **cardiac tests** for all patients with cardiac risk factors or patients at or above the threshold dose levels [Echocardiograms, WMS studies, and/or all angiography scans]
- Baseline **liver function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]

CARDIAC

0 None

1 —

- 2 Asymptomatic, resting ejection fraction decline by $>10\%$ baseline, or abnormal cardiac function tests (LVEF >50) with no baseline for comparison
- 3 Mild Congestive Heart Failure, responds to therapy
- 4 Severe/refractory Congestive Heart Failure

At cumulative dose threshold and subsequent intervals

For Cardiac Toxicity Ratings

First rating at baseline, then at the cumulative dose **threshold** of 300mg/m^2 & repeat ratings at each cumulative dose **increment** of 100mg/m^2 above threshold (Cumulative dose sooner for high risk patients, eg pre-existing cardiac disease, prior chest irradiation)

Note: Threshold Cumulative dose reduced proportionately if other anthracycline or anthracenedione drugs have been given, cardiotoxicity is additive

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT

Approx. 30 minutes

SA-IFN***KAP**

Interferon Chemotherapy

(Kaposi's Sarcoma- Indolent Disease-
Palliative Intent)

Take-Home Prescription-
Special Authorization Required

INTERFERON ALFA 3MU/m² SC Three Times Weekly

(Outpatient prescription in multiples of 3MU vials)

CONTINUOUS TREATMENT TO RESPONSE

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC), liver function tests (Serum alkaline phosphatase, GGT, ALT, AST & Bilirubin) and serum glucose levels twice weekly

LETHARGY

- 0. None
- 1. Mild (Performance Status decreased by 1)
- 2. Moderate (Performance Status decreased by 2)
- 3. Severe (Performance Status decreased by 3)

Rated at weekly clinic visit

FLU-LIKE SYMPTOMS

- 0. None
- 1. Mild
- 2. Moderate
- 3. Severe

(*Arthralgia, myalgia,
diaphoresis, rigours/
chills*)

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: NOT APPLICABLE

- Routine prophylaxis of flu-like symptoms with Acetaminophen 325-500mg tablets 1 or 2 tablets before each dose (especially if this adverse effect occurs with early doses)

NOTE

Prescription costs covered by most third party prescription plans, for *Pharmacare* approval the prescriber must write a letter of request for each patient

SA-IFOS-1D

Ifosfamide Chemotherapy

(Soft Tissue Sarcoma- Palliative
Intent)

ADVANCED LEVEL REGIMEN-
Provincial Cancer Centre

PREHYDRATION

- Normal Saline 1000mL infuse over 1 hour

MESNA 600mg/m² IV Day 1 immediately before Ifosfamide

- Dilute in 50mL minibag (Normal Saline); Infuse over 15 minutes

IFOSFAMIDE 5000mg/m² CIV Day 1(Round to nearest 100mg. Usually given in hospital)

- Dilute in 1000mL bag (Normal Saline); Infuse over 24 hours
- May give concurrent hydration with 1-3L of IV fluid during infusion, to maintain high urine flow

MESNA 5000mg/m² CIV Day 1

- Dilute in 1000mL bag (Normal Saline)- Admix in same bag as Ifosfamide; Infuse over 24 hours concurrent with Ifosfamide

MESNA 2500mg/m² CIV Day 2

- Dilute in 2 x 1000mL bags (Normal Saline); Infuse over 12 hours immediately following Ifosfamide infusion

POSTHYDRATION

- May give Normal Saline 1000mL infuse over 1 hour

REPEAT EVERY 28 DAYS For a Usual Total of 2 to 4 Cycles

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-200mg PO or 100mg IV), **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)
- Consider also a Neurokinin-1 Receptor Antagonist (Aprepitant 125 mg PO) *"When available in Canada"*

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses. **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for 1-2 days, if given pre-chemo
- Consider also a Neurokinin-1 Receptor Antagonist if given pre-chemo (Aprepitant 80 mg PO q 24 hours for 3 days) *"When available in Canada"*
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration
- Inadequate total hydration may result in dose-related hemorrhagic cystitis

SA-IFOS-1D

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Urinalysis (for RBCs/HPF) before each cycle of treatment
- Baseline & periodic **hepatic function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]
- Baseline & periodic **renal function tests** [serum creatinine, serum electrolytes & BUN]
- **Neurologic toxicity ratings** (Cortical) at each visit

CYSTITIS

0. None
1. Mild symptoms
2. Symptoms relieved with therapy
3. Symptoms not relieved
4. Life-threatening

CORTICAL

1. None
2. Mild somnolence
3. Moderate somnolence
4. Severe somnolence, confusion, hallucination
5. Coma, seizures

Rated at each clinic or hospital visit

DOSE MODIFICATION

Urologic Toxicities

1. If RBC/HPF > 10, notify physician, **HOLD** Ifosfamide and continue Mesna

Hematologic Toxicities

1. If ANC < $1.5 \times 10^9/L$, or if Platelets < $100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Renal failure (Recommended action)

1. If CrCl < 30mL/min or Serum Creatinine > 185µmol/L, **reduce** Ifosfamide to 75% dose
2. If CrCl < 12mL/min, **reduce** Ifosfamide to 50% dose

Hepatic dysfunction (Suggested action)

1. If Bili=26-51mmol/L or AST=60-180IU/L **reduce** Ifosfamide to 75% dose
2. If Bili= 52-85mmol/L, **reduce** Ifosfamide to 50% dose

PHYSICIAN'S STANDING ORDERS AVAILABLE FOR THIS REGIMEN

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:

Days 1&2- Approx. 30 minutes (if given by CADD pumps)

**Ifosfamide Low Dose
Chemotherapy**

(Soft Tissue Sarcoma- Palliative
Intent)

**ADVANCED LEVEL REGIMEN-
Provincial Cancer Centre**

PREHYDRATION

- Encourage patient to drink 6-8 glasses of water prior to chemo each day
- May give 500mL Normal Saline; Infuse over 1 hour before chemotherapy each day

**IFOSFAMIDE 1800mg/m² IV Days 1 to 5 (Round to nearest 100mg)
WITH**

MESNA 360mg/m² IV Days 1 to 5

- Admix Ifosfamide and Mesna together in 500mL bag (Normal Saline)-
Infuse over 3 hours
- May hydrate with 1-3L of IV fluid during infusion, to maintain high urine
flow

MESNA 360mg/m² IV 4 & 8 hours after each Ifosfamide dose- Days 1 to 5

- Dilute in 50mL bag (Normal Saline); Infuse over 15 minutes

POSTHYDRATION

- May give 500mL Normal Saline; Infuse over 1 hour after Ifosfamide/Mesna
infusion each day

REPEAT EVERY 21 DAYS *For a Usual Total of 2 to 4 Cycles*

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: HIGH RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist (Ondansetron 8mg PO- may substitute
Ondansetron 8mg IV, or Granisetron 2mg PO or 1mg IV, or Dolasetron 100-
200mg PO or 100mg IV), **AND**
- Dexamethasone 8mg PO (may increase to 20mg PO or IV)

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 3 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if
given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron
given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1-2 days, or Dolasetron 100mg PO q24h for
1-2 days, if given pre-chemo
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN
or Metoclopramide 10mg PO q4h)
- Oral hydration is strongly encouraged; poorly hydrated patients may need
more IV hydration
- Inadequate total hydration may result in dose-related hemorrhagic cystitis

SA-IFOS-5D

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Baseline and daily **urinalysis** (for RBCs/HPF) for 5 days during treatment
- Baseline & periodic **hepatic function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]
- Baseline & periodic **renal function tests** [serum creatinine, serum electrolytes & BUN]
- **Neurologic toxicity ratings** (Cortical) at each visit

CYSTITIS

- 0 None
- 1 Mild symptoms
- 2 Symptoms relieved with therapy
- 3 Symptoms not relieved
- 4 Life-threatening

CORTICAL

- 1 None
- 2 Mild somnolence
- 3 Moderate somnolence
- 4 Severe somnolence, confusion, hallucination
- 5 Coma, seizures

Rated at each clinic or hospital visit

DOSE MODIFICATION

Urologic Toxicities

- 1 If RBC/HPF > 10, notify physician.
HOLD Ifosfamide and continue Mesna

Hematologic Toxicities

1. If ANC < $1.5 \times 10^9/L$, or if Platelets < $100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Renal failure (Recommended action)

- 1 If CrCl < 30mL/min or Serum Creatinine > $185 \mu\text{mol/L}$, **reduce** Ifosfamide to 75% dose
- 2 If CrCl < 12mL/min, **reduce** Ifosfamide to 50% dose

Hepatic dysfunction (Suggested action)

- 1 If Bili = 26-51mmol/L or AST = 60-180IU/L **reduce** Ifosfamide to 75% dose
- 2 If Bili = 52-85mmol/L, **reduce** Ifosfamide to 50% dose

PHYSICIAN'S STANDING ORDERS AVAILABLE FOR THIS REGIMEN

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT:

Days 1&2- Approx. 30 minutes (if given by CADD pumps)

SA-IFOS-W

Weekly Ifosfamide Chemotherapy

(Soft Tissue Sarcoma- Palliative
Intent)

ADVANCED LEVEL REGIMEN-
Provincial Cancer Centre

PREHYDRATION

- Encourage patient to drink 6-8 glasses of water prior to chemo each day

MESNA 150mg/m² IV before Ifosfamide infusion

- Dilute IV dose in 100mL bag (Normal Saline); Infuse over 15 minutes

IFOSFAMIDE 1500mg/m² CIV Day 1 over 24 hours (Round to nearest 100mg)

- Dilute in 1000mL bag (Normal Saline); Infuse over 24 hours
- May be given by continuous infusion over 24 hours using CADD pump
- Oral or IV hydration with 1-3L of IV fluid during infusion, to maintain high urine flow

MESNA 1200mg/m² CIV over 24 hours with Ifosfamide

- Admix CIV dose with Ifosfamide, as above; may be infused using a CADD ambulatory infusion pump

REPEAT EVERY 7 DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: INTERMEDIATE RISK

Pre-Chemotherapy-

- Dexamethasone 4-8 mg PO, and/or
- Dopamine Receptor Antagonist PO (e.g. Metoclopramide 10-20mg PO, or Prochlorperazine 10mg PO)

Post-Chemotherapy-

- Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10mgPO q3-4h PRN

OTHER SUPPORTIVE CARE

- Oral hydration is strongly encouraged: poorly hydrated patients may need more IV hydration
- Inadequate total hydration may result in dose-related hemorrhagic cystitis

SA-IFOS-W

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Baseline and weekly **urinalysis** (for RBCs/HPF) during treatment
- Baseline & periodic **hepatic function tests** [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]
- Baseline & periodic **renal function tests** [serum creatinine, serum electrolytes & BUN]
- **Neurologic toxicity ratings** (Cortical) at each visit

CYSTITIS

- 0 None
- 1 Mild symptoms
- 2 Symptoms relieved with therapy
- 3 Symptoms not relieved
- 4 Life-threatening

CORTICAL

- 1 None
- 2 Mild somnolence
- 3 Moderate somnolence
- 4 Severe somnolence, confusion, hallucination
- 5 Coma, seizures

Rated at each clinic visit

DOSE MODIFICATION

Urologic Toxicities

1. If RBC/HPF > 10, notify physician,
HOLD Ifosfamide and continue Mesna

Hematologic Toxicities

1. If ANC < $1.5 \times 10^9/L$, or if Platelets < $100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Renal failure (Recommended action)

1. If CrCl < 30mL/min or Serum Creatinine > 185µmol/L, **reduce** Ifosfamide to 75% dose
2. If CrCl < 12mL/min, **reduce** Ifosfamide to 50% dose

Hepatic dysfunction (Suggested action)

1. If Bilirubin = 26-51mmol/L or AST = 60-180IU/L **reduce** Ifosfamide to 75% dose
2. If Bilirubin = 52-85mmol/L, **reduce** Ifosfamide to 50% dose

PHYSICIAN'S STANDING ORDERS AVAILABLE FOR THIS REGIMEN

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT
Approx. 30 minutes (if given by ambulatory pump)

SA-IFOS-ETOP

Ifosfamide-Etoposide

Chemotherapy

(Ewing's Sarcoma/Osteogenic
Sarcoma - Palliative Intent)

ADVANCED LEVEL REGIMEN-
Provincial Cancer Centre

PREHYDRATION

- Encourage patient to drink 6-8 glasses of water prior to chemo each day
- May give 500mL Normal Saline; Infuse over 1 hour before chemotherapy each day

ETOPOSIDE 100mg/m² IV Days 1 to 5 (Round to nearest 10mg)

- Admix in 500mL bags of Normal Saline; Infuse over 60 minutes (Hour 0-1), BEFORE Ifosfamide

IFOSFAMIDE 1800mg/m² IV Days 1 to 5 (Round to nearest 100mg)

WITH

MESNA 360mg/m² IV Days 1 to 5

- Admix Ifosfamide and Mesna together in 500mL bag (Normal Saline)- Infuse over 3 hours (Hours 1-4) AFTER Etoposide
- May hydrate with 1-3L of IV fluid during infusion, to maintain high urine flow

MESNA 360mg/m² IV 4 & 8 hours after each Ifosfamide dose- Days 1 to 5

- Dilute in 50mL bag (Normal Saline); Infuse over 15 minutes (in Hour 5 and Hour 9)

OR

MESNA 720mg/m² PO daily mixed in juice, 4 & 8 hours after Ifosfamide

- Important Note: If oral MESNA dose lost in emesis (within 30 minutes of dose), repeat oral dose, or use IV MESNA replacement dose

REPEAT EVERY 28 DAYS

DOSE MODIFICATION

Urologic Toxicities

1. If RBC > 10 HPF, notify physician, **HOLD** Ifosfamide and continue Mesna

Hematologic Toxicities

1. If ANC < 1.5 x 10⁹/L, or if Platelets < 100 x 10⁹/L, notify physician and **HOLD** dose for 1 week

Renal failure (Recommended action)

1. If CrCl = 12-48mL/min or Serum Creatinine > 130µmol/L, reduce Etoposide to **75%** dose
2. If CrCl < 12mL/min, reduce Etoposide to **50%** dose
3. If Serum Creatinine > 200µmol/L, **reduce** Ifosfamide to **75%** dose
4. If Serum Creatinine > 300µmol/L, **reduce** Ifosfamide to **67%** dose

Hepatic dysfunction (Suggested action)

1. If Bili = 26-51µmol/L or AST = 60-180IU/L, **reduce** Etoposide to **50%** dose
2. If Bili = 52-85µmol/L or AST > 180IU/L, **reduce** Etoposide to **25%** dose
3. If Bili > 85µmol/L, **OMIT** Etoposide dose
4. Consider Ifosfamide dose reduction if LFTs elevated (eg. Bilirubin or AST)

PHYSICIAN'S STANDING ORDERS
AVAILABLE FOR THIS REGIMEN

Continued Next Page...

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: INTERMEDIATE RISK

Pre-Chemotherapy-

- Serotonin Receptor Antagonist IV (Ondansetron 8mg IV pre-chemo & 8mg PO qhs on Days 1 to 5, OR Granisetron 1mg IV pre-chemo Days 1 to 5, OR Dolasetron 100mg IV pre-chemo Days 1 to 5), **AND**
- Dexamethasone 8mg IV pre-chemo Days 1 to 5 (may increase to 20mg PO or IV)

Post-Chemotherapy-

- Dexamethasone 8 mg PO q24h for 2 doses, **AND**
- Serotonin Receptor Antagonist PO (Ondansetron 8mg PO q12h for 3 doses if given prechemo) **OR**
 - No post-chemo serotonin receptor antagonist if Granisetron or Dolasetron given pre-chemo **OR**
 - Granisetron 2mg PO q24h for 1 day, or Dolasetron 100mg PO q24h for 1 day, if given pre-chemo
- Dopamine Receptor Antagonist PRN (Prochlorperazine 10mg PO q4-6h PRN or Metoclopramide 10mg PO q4h)

OTHER SUPPORTIVE CARE

- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration
- Inadequate total hydration may result in dose-related hemorrhagic cystitis
- If previous episode of febrile neutropenia, give Filgrastim 5µg/Kg SC daily following chemotherapy

HYPERSENSITIVITY REACTION

- Follow hypersensitivity management protocol
- Give Diphenhydramine 50mg IV push & Hydrocortisone 100mg IV push

SA-IFOS-ETOP

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Baseline and daily urinalysis (for RBCs) for 5 days during treatment
- Clinical assessment of stomatitis: oral examination upon patient complaint of a sore mouth
- Baseline blood pressure at each treatment; monitor for hypotension
- Baseline & periodic hepatic function tests [serum alkaline phosphatase, GGT, ALT, AST & Bilirubin levels- serum proteins may be added if indicated]
- Baseline & periodic renal function tests [serum creatinine, serum electrolytes (including Ca^{2+} & Mg^{2+}) & BUN], on Days 1 & 3 of each chemotherapy cycle
- Neurologic toxicity ratings (Cortical) at each visit

CYSTITIS

- 0 None
- 1 Mild symptoms
- 2 Symptoms relieved with therapy
- 3 Symptoms not relieved
- 4 Life-threatening

CORTICAL

1. None
2. Mild somnolence
3. Moderate somnolence
4. Severe somnolence, confusion, hallucination
5. Coma, seizures

Rated at each clinic visit

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT

Days 1-5- Usually inpatient

If outpatient, approx 3-4 hours
(followed by ambulatory pump)

SA-VINBLAST

Vinblastine Chemotherapy

(Kaposi's Sarcoma- Palliative Intent)

INTERMEDIATE LEVEL REGIMEN-

Regional Hospital with Dedicated
Cancer Treatment Unit

VINBLASTINE 10mg IV Day 1(Round to nearest 0.1mg)

- Quick push through sidearm of free flowing IV (Normal Saline); Inject over 1 minute

REPEAT EVERY 7 (or 14) DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic before chemotherapy
- After chemotherapy use
Prochlorperazine 10mg PO q4-6h
PRN or Metoclopramide 10mgPO
q3-4h PRN

DOSE MODIFICATION

Hematologic Toxicities

- 1 If ANC $< 1.5 \times 10^9/L$ or if Platelets $< 100 \times 10^9/L$ notify physician and **HOLD** dose for 1 week

Hepatic dysfunction (Recommended action)

- 1 If Bili= 25-50 μ mol/L or AST= 60-180IU/L **reduce** to **50%** dose
- 2 If Bili $> 50\mu$ mol/L or AST > 180 IU/L, **reduce** to **25%** dose

Neurotoxicity (Suggested action)

- 1 If Neurotoxicity $\geq$ Grade 2. **HOLD** dose for 1 week or until resolved
- 2 If severe paresthesia or foot drop, **reduce** to **50%** dose

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Neurologic toxicity ratings (Sensory) at each visit

SENSORY

- 0 No change
- 1 Mild paraesthesia, no deep tendon reflex
- 2 Mild/mod sensory loss; mod paraesthesia
- 3 Sensory loss interferes with function

Rated at each clinic visit

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT

Approx. 30 minutes

SA-VINCRIST

Vincristine Chemotherapy

(Kaposi's Sarcoma- Palliative Intent)

INTERMEDIATE LEVEL REGIMEN-

Regional Hospital with Dedicated
Cancer Treatment Unit

VINCRISTINE 2mg IV Day 1 (Round to nearest 0.1mg)

- Push through sidearm of free flowing IV; Inject over at least 1 minute

REPEAT EVERY 7 (or 14) DAYS

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: LOW RISK

- No routine antiemetic before chemotherapy
- After chemotherapy, use Prochlorperazine 10mg PO q4-6h PRN, or Metoclopramide 10mgPO q3-4h PRN

DOSE MODIFICATION

Hematologic Toxicities

1. If ANC < $1.5 \times 10^9/L$, or if Platelets < $100 \times 10^9/L$, notify physician and **HOLD** dose for 1 week

Hepatic dysfunction (Recommended action)

1. If Bilirubin = 25-50 $\mu\text{mol/L}$ or AST = 60-180 IU/L, **reduce** to 50% dose
2. If Bilirubin > 50 $\mu\text{mol/L}$ or AST > 180 IU/L, **reduce** to 25% dose

Neurotoxicity (Suggested action)

1. If Neurotoxicity $\geq$ Grade 2, **HOLD** dose for 1 week or until resolved
2. If severe paresthesia or foot drop, **reduce** to 50% dose

CLINICAL MONITORING

- Complete blood count including differential, platelets and hemoglobin (CBC) before each cycle of treatment
- Neurologic toxicity ratings (Sensory) at each visit
- Constipation toxicity ratings before each Vincristine treatment

SENSORY

- 0 No change
- 1 Mild paraesthesia, no deep tendon reflex
- 2 Mild/moderate sensory loss, moderate paraesthesia
- 3 Sensory loss interferes with function

CONSTIPATION

- 0 No change
 - 1 Mild
 - 2 Moderate
 - 3 Severe
 - 4 Ileus > 96 hours
- Rated at each clinic visit**

PATIENT VISIT

CHEMOTHERAPY PATIENT VISIT

Approx 30 minutes

REGIMEN CONTENTS

AMIFOS - <i>Amifostine Supportive Therapy</i>	
CALCITONIN - <i>Calcitonin Supportive Therapy</i>	
CLOD*IV - <i>Clodronate Supportive Therapy</i>	
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NOTE: Regimen names in *italics* are not in this pocketbook version- See full version for regimen monograph

DEXRAZOX

DEXRAZOXANE Supportive Therapy

(Protection Against Doxorubicin-Related Cardiotoxicity)

INTERMEDIATE LEVEL REGIMEN-
Regional Hospital with Dedicated
Cancer Treatment Unit

DEXRAZOXANE 500mg/m² IV over 15 minutes

Or dose may be calculated at a 10:1 ratio with the Doxorubicin dose

- Mix to a total volume of 100mL solution (5% Dextrose or Normal Saline) and infuse over 15 minutes
- Start dose 30 minutes BEFORE planned start time for Doxorubicin, begin Doxorubicin treatment 15 minutes after Dexrazoxane infusion completed

REPEAT WITH EVERY DOXORUBICIN DOSE

SUPPORTIVE CARE

ANTIEMETIC REGIMEN:

- As required for chemotherapy regimen

CLINICAL MONITORING

- As per chemotherapy regimen

PATIENT VISIT

Approximately 15 minutes addition to duration of visit for Chemotherapy Administration

CHEMOAPPOINTMENT TYPE - No change from Appointment Type for chemotherapy regimen

**EPOIETIN****EPOIETIN Supportive Therapy***(Prevention or treatment of Anemia)***Take-Home Prescription-
Special Authorization Required****BASIC LEVEL REGIMEN-
Community Hospital with
Oncology Nurses****EPOIETIN 150IU/Kg** three times weekly SC

- Evaluate iron status at baseline and during Epoietin treatment
- Evaluate hemoglobin after 4 weeks' treatment, if hemoglobin increased by $\geq 10\text{g/L}$, continue initial dose of Epoietin
- If hemoglobin increased by $< 10\text{g/L}$, may increase to 300IU/Kg three times weekly
- If hemoglobin increased by $> 20\text{g/L}$ or if hemoglobin exceeds 140g/L, may decrease dose by 25%

Alternate Dosing: 40,000 IU SC once weekly

(Outpatient prescription in multiples of 20,000IU & 40,000IU vials)

- Round to nearest vial size, if possible
- Re-evaluate the need for epoietin when chemotherapy is completed

SUPPORTIVE CARE**ANTIEMETIC REGIMEN: NONE****CLINICAL MONITORING**

- Regular monitoring of Hgb results (every 2-4 weeks) until target Hgb of 110-120g/L is maintained

NOTES

- Prescription covered by some private third party prescription plans. prescriptions submitted to Seniors' Pharmacare patients must include a specific non-formulary request form on initial application and monitoring forms during continuing therapy
- Dispense medication with adequate number of syringes, needles, alcohol swabs and other equipment for patient self-injection. Store this medication under refrigeration

Pharmacare Formulary Restrictions for Epoietin Approval

1. Patients with hematologic malignancies who require frequent blood transfusions and who are at risk of iron overload from transfusions
 - Baseline Hgb $\leq 90\text{g/L}$
 - Require ≥ 2 transfusions per month
 - Initial 12 weeks' treatment, renewed on completion of Monitoring Form and evidence of response and minimized transfusion requirements

FENT*DERM

Transdermal FENTANYL Therapy

Take-Home Prescription-
Special Authorization Required

Systemic Pain (Cancer or therapy-related): Poor Tolerance to Oral Opioid Analgesics

Transdermal FENTANYL dose to analgesic response

Affix to skin q72h (3 days)

(Outpatient prescription in boxes of 5 patches of Duragesic -25, 50, 75 or 100µg/hr)

- Usually pain is stabilized on oral analgesics (e.g. Morphine or Hydromorphone) before conversion to Transdermal Fentanyl. Convert dose by adding total Morphine (or equivalent) over 24 hours, then select starting dose from table. Continue oral analgesics for 12-24 hours after starting Transdermal Fentanyl, to allow for slow onset of action. Adjust dose to analgesic response. Allow 1-2 days between each dose level change, to assess response
- May titrate to full or partial pain relief, as possible and as agreed with the patient
- May give additional oral analgesic doses (immediate release) for breakthrough pain: Breakthrough doses (BTD) usually 10% of 24 hour oral Morphine equivalent
- Usually given to a maximum of 300µg/hr dose

CONTINUOUS TREATMENT

NOTES

- Narcotic prescription which requires a written prescription on triplicate prescription form for each filling; may order total quantity in split fractions to be dispensed at specific intervals. Always indicate total amount to dispense
- May order in different strengths for a target dosage
- Ensure that adequate bowel regimen, usually including laxatives (stool softener and bowel irritant), is in place through treatment with Transdermal Fentanyl (even though treatment is not oral)
- Duragesic® available through most third party prescription insurers; for Pharmacare patients, a special letter of request will be required from the prescriber

CLINICAL MONITORING

- Regular monitoring of pain levels and response to analgesics, to determine whether the dose requires modification

Pain

- 0 None
- 1 Mild
- 2 Discomforting
- 3 Distressing
- 4 Horrible
- 5 Excruciating

Pain-Response to Analgesics

- 0 None (or pain worse than before)
- 1 No relief
- 2 Slight relief
- 3 Moderate relief
- 4 Substantial relief
- 5 Complete relief

FENT*DERM

DOSE CONVERSION

Conversion of Oral Morphine to Transdermal Fentanyl*

Oral Morphine	Fentanyl	Oral Morphine	Fentanyl
30 to 90	25	391 to 450	175
91 to 150	50	451 to 510	200
151 to 210	75	511 to 570	225
211 to 270	100	571 to 630	250
271 to 330	125	631 to 690	275
331 to 390	150	691 to 750	300

* about 50% of patients will require further dose increases after conversion

FILGRASTIM

FILGRASTIM Supportive Therapy

(Prevention or treatment of Febrile
Neutropenia)

Take-Home Prescription-
Special Authorization Required

FILGRASTIM 5mcg/Kg daily SC for 7 to 10 days (until
neutrophil recovery)

(Outpatient prescription in multiples of 300µg & 480µg vials)

- Start treatment 24 hours AFTER last myelosuppressive chemotherapy dose given (NB includes oral chemotherapy doses)
- Round to nearest vial size, if possible
- May give Acetaminophen 1-2 tablets for temporary bone pain at initiation of treatment

For a Usual Duration of 5-10 days, or until $ANC \geq 10 \times 10^9/L$

SUPPORTIVE CARE

ANTIEMETIC REGIMEN NONE

CLINICAL MONITORING

- Regular monitoring of CBC results (once or twice weekly) until recovery of ANC

NOTES

- Prescription covered by provincial plan for patients without third party prescription insurance- all doses provided by QEII Health Sciences Centre Pharmacy
- Prescription covered by private third party prescription plans; Seniors' Pharmacare patients must utilize provincial plan
- Dispense medication with adequate number of syringes, needles, alcohol swabs and other equipment for patient self-injection. Store this medication under refrigeration

Formulary Restrictions for Filgrastim Approval

1. secondary prophylaxis of febrile neutropenia (FN) in patients with prior episode FN subsequent to chemotherapy;
2. patients unable to tolerate chemotherapy due to dose reduction or delay where dose intensity is important;
3. chronic neutropenia;
4. patients prior to peripheral blood cell collection;
5. following autologous transplant, patients receiving allogeneic BMT to accelerate engraftment;
6. patients with drug induced neutropenia from AIDS therapy;
7. patients with chronic neutropenia while awaiting BMT (e.g. myelodysplastic disorders, aplastic anemia);
8. primary prevention with standard chemotherapy where there is $\geq 50\%$ febrile neutropenia rate (documented)

HYDROMORPH*PO

Oral HYDROMORPHONE Therapy

Take-Home Prescription-
Unrestricted

HYDROMORPHONE (immediate release)

dose to analgesic response PO q4-6h (usually q4h)

(Outpatient prescription in tablets- Hydromorphone -1, 2, 4, or 8mg)

HYDROMORPHONE (sustained release)

dose to analgesic response PO q8-12h (usually q12h)

(Outpatient prescription in tablets- Hydromorph Contin-3, 6, 12, or 24mg)

- May titrate to full or partial pain relief, as possible and as agreed with the patient
- If pain is periodic, give Hydromorphone PRN; if pain is continuous, give Hydromorphone routinely
- May give additional doses for breakthrough pain. Breakthrough doses (BTD) usually a to $\frac{1}{2}$ q4h dose given q1-2h, to allow dosage up to 2x q4h dose (or, may give 10% of 24 hour dose for BTD)
- Doses given around-the-clock for continuous severe pain, may double up bedtime dose and skip middle of the night dose, if pain relief is sustained all night
- If pain control is stable, convert to Hydromorphone Sustained Release tablets q12h (at 3x q4h dose), with appropriate BTD of immediate release Hydromorphone tablets

CONTINUOUS TREATMENT

NOTES -

- Narcotic prescription which requires a written prescription on triplicate prescription form for each filling, may order total quantity in split fractions to be dispensed at specific intervals. Always indicate total amount to dispense
- May order in different strengths for a target dosage, or for routine and breakthrough doses
- As a 'rule of thumb', Morphine/Hydromorphone potency is 5:1; when converting from a Morphine dose to a Hydromorphone dose, divide the Morphine dose by 5 to calculate the Hydromorphone dose
- Ensure that adequate bowel regimen, usually including laxatives (stool softener and bowel irritant), is in place through treatment with Hydromorphone
- Hydromorph Contin® available through most third party prescription insurers; for Pharmacare patients, a special letter of request will be required from the prescriber

HYDROMORPH*PO

DOSE TITRATION

Titration of Hydromorphone Doses

1. Step method by set amounts given q4h
 - 2-3-4-6-8-10-12-16-20-24-36-44-60-80 mg
2. By frequency of breakthrough doses (BTD)
 - 1-2 BTD per day- no change in dose
 - ≥ 3 BTD per day + full relief - increase regular dose by BTD amount
 - No relief - Triple regular dose
3. Total daily dosage method
 - Add total mg given over 24 hours, including BTD
 - Divide by 6 for q4h dosing, and give for next 2 days
 - Recalculate and order new BTD at $\frac{1}{2}$ of regular dose
4. Percent incremental method
 - Increase each 24 hours by percentage amount:
 - No relief (0-1)- 100% increase
 - Minor relief (2-3)- 50% increase
 - Mostly relieved (4) - 25% increase
 - Full relief (5)- 0% increase

CLINICAL MONITORING

- Regular monitoring of pain levels and response to analgesics, to determine whether the dose requires modification

Pain

0. None
1. Mild
2. Discomforting
3. Distressing
4. Horrible
5. Excruciating

Pain-Response to Analgesics

0. None (or pain worse than before)
1. No relief
2. Slight relief
3. Moderate relief
4. Substantial relief
5. Complete relief

MORPH*PO

Oral MORPHINE Therapy

Take-Home Prescription-
Unrestricted

MORPHINE (immediate release)

dose to analgesic response PO q4-6h (usually q4h)

(Outpatient prescription in tablets- 5, 10, 20, 25, 30, 40, 50, 60mg)

MORPHINE (sustained release)

dose to analgesic response PO q8-12h (usually q12h)

(Outpatient prescription in tablets or capsules- Morphine Sulphate- 15, 30, 60, 100, 200mg; or Kadian 20, 50, 60mg q24h)

- May titrate to full or partial pain relief, as possible and as agreed with the patient
- If pain is periodic, give Morphine PRN; if pain is continuous, give Morphine routinely
- May give additional doses for breakthrough pain: Breakthrough doses (BTD) usually a to $\frac{1}{2}$ q4h dose given q1-2h, to allow dosage up to 2x q4h dose (or, may give 10% of 24 hour dose for BTD)
- Doses given around-the-clock for continuous severe pain; may double up bedtime dose and skip middle of the night dose, if pain relief is sustained a night
- If pain control is stable, convert to Morphine Sustained Release tablets q12h (at 3x q4h dose), with appropriate BTD of immediate release Morphine tablets

CONTINUOUS TREATMENT

NOTES

- Narcotic prescription which requires a written prescription on triplicate prescription form for each filling; may order total quantity in split fractions to be dispensed at specific intervals. Always indicate total amount to dispense
- May order in different strengths for a target dosage, or for routine and breakthrough doses
- Ensure that adequate bowel regimen, usually including laxatives (stool softener and bowel irritant), is in place through treatment with Morphine

MORPH*PO

DOSE TITRATION

Titration of Morphine Doses

1 Step method by set amounts given q4h

- 10-15-20-30-40-50-60-80-100-120-180-220-300-400 mg

2 By frequency of breakthrough doses (BTD)

- 1-2 BTD per day- no change in dose

- ≥ 3 BTD per day + full relief - increase regular dose by BTD amount

- No relief - Triple regular dose

3 Total daily dosage method

- Add total mg given over 24 hours, including BTD

- Divide by 6 for q4h dosing, and give for next 2 days

- Recalculate and order new BTD at $\frac{1}{2}$ of regular dose

4 Percent incremental method

- Increase each 24 hours by percentage amount:

- No relief (0-1)- 100% increase

- Minor relief (2-3)- 50% increase

- Mostly relieved (4) - 25% increase

- Full relief (5)- 0% increase

CLINICAL MONITORING

- Regular monitoring of pain levels and response to analgesics, to determine whether the dose requires modification

Pain

0. None

1. Mild

2. Discomforting

3. Distressing

4. Horrible

5. Excruciating

Pain-Response to Analgesics

0. None (or pain worse than before)

1. No relief

2. Slight relief

3. Moderate relief

4. Substantial relief

5. Complete relief

OCTREO

OCTREOTIDE Supportive Therapy

(Bowel Obstruction Management-
Palliative Intent)

Take-Home Prescription-
Special Authorization Required

OCTREOTIDE 50-150mcg BID - TID SC

(Outpatient prescription in multiples of 50mcg, 150mcg & 500mcg vials)

CONTINUOUS TREATMENT

SUPPORTIVE CARE

ANTIEMETIC REGIMEN: NONE

CLINICAL MONITORING

- Baseline and periodic serum glucose levels, especially in diabetic patients
- Ultrasonograph of the gall bladder, to assess the presence of gallstones (during long-term therapy)

NOTES

- Prescription covered by some third party prescription plans.
- Dispense medication with adequate number of syringes, needles, alcohol swabs and other equipment for patient self-injection

**PAMID****PAMIDRONATE Supportive Therapy**

*Hypercalcemia
(Cancer or therapy-related)*

BASIC LEVEL REGIMEN-
Community Hospital with
Oncology Nurses

PAMIDRONATE 60 to 90mg IV over 2-4 hours
(over 2 hours if CrCl <180mmol/L)

- If Corrected Serum Calcium* = **2.7-3.5 mmol/L**, give **60mg**

60mg Dose: Mix in 250-500mL solution (5% Dextrose, Normal Saline) and infuse over 2 hours

- If Corrected Serum Calcium* >**3.5 mmol/L**, give **90mg**
(If Ca = 3.0-3.5 give 30-60mg; if Ca = 3.5-4.0, give 60-90mg)

90mg Dose: Mix in 500-1000mL solution (5% Dextrose, Normal Saline) and infuse over 4 to 6 hours

- Admix into 250mL or 500mL ambulatory pump & infuse over 2-5 hours at home for subsequent doses (Intermate LV 50 or LV 250 pump)

*Corrected Serum Calcium = Measured Serum Calcium + [(40 - Serum Albumin) x 0.02]

REPEAT EVERY 14 to 28 DAYS

Until Normalization of Serum Calcium Levels

CLINICAL MONITORING

- Serum electrolytes, including calcium

Hypocalcemia

0. Serum Calcium >2.10 µmol/L
1. Serum Calcium =2.10 to 1.93 µmol/L
2. Serum Calcium =1.92 to 1.74 µmol/L
3. Serum Calcium =1.73 to 1.51 µmol/L
4. Serum Calcium <1.50 µmol/L

Rated on assessment of anti-hypercalcemia response and at periodic visits or in response to patient complaint

NOTESExpected Clinical Outcomes

- Assessment of Serum Calcium at 3 to 7 days after treatment; rating of response by Response Criteria
- No retreatment if patient is normocalcemic, or only mildly hypercalcemic (use clinical judgement)

Hypercalcemia- Response Criteria

0. Serum Calcium <2.64 µmol/L
1. Serum Calcium =2.64 to 2.88 µmol/L
2. Serum Calcium =2.89 to 3.12 µmol/L
3. Serum Calcium =3.13 to 3.37 µmol/L
4. Serum Calcium >3.37 µmol/L

Rated on assessment of anti-hypercalcemia response and at periodic visits or in response to patient complaint

PATIENT VISIT

Approximately 2 hours (60mg) to 4 hours (90mg)

OR: 15minutes for ambulatory pump

**ZOLED****ZOLEDRONIC ACID****Supportive Therapy**

Hypercalcemia

(Cancer or therapy-related)

BASIC LEVEL REGIMEN-Community Hospital with
Oncology Nurses**ZOLEDRONATE 4mg IV over 5 minutes**May increase to **8mg** if hypercalcemia control inadequate after previous dose

- Inject into sidearm of free-flowing IV over 5 minutes

REPEAT EVERY 14 to 28 DAYS*Until Normalization of Serum Calcium Levels***CLINICAL MONITORING**

- Serum electrolytes, including calcium
- Hypocalcemia

0. Serum Calcium $>2.10 \mu\text{mol/L}$
1. Serum Calcium $=2.10$ to $1.93 \mu\text{mol/L}$
2. Serum Calcium $=1.92$ to $1.74 \mu\text{mol/L}$
3. Serum Calcium $=1.73$ to $1.51 \mu\text{mol/L}$
4. Serum Calcium $<1.50 \mu\text{mol/L}$

Rated on assessment of anti-hypercalcemia response and at periodic visits or in response to patient complaint

GUIDELINE

See the CCNS Website
www.cancercare.ns.ca for the
guideline on Zoledronate for tumour-
induced Hypercalcemia

NOTESExpected Clinical Outcomes

- Assessment of Serum Calcium at 3 to 7 days after treatment, rating of response by Response Criteria
- No retreatment if patient is normocalcemic, or only mildly hypercalcemic (use clinical judgement)

Hypercalcemia- Response Criteria

0. Serum Calcium $<2.64 \mu\text{mol/L}$
1. Serum Calcium $=2.64$ to $2.88 \mu\text{mol/L}$
2. Serum Calcium $=2.89$ to $3.12 \mu\text{mol/L}$
3. Serum Calcium $=3.13$ to $3.37 \mu\text{mol/L}$
4. Serum Calcium $>3.37 \mu\text{mol/L}$

Rated on assessment of anti-hypercalcemia response and at periodic visits or in response to patient complaint

PATIENT VISIT

Approximately 2 hours (60mg) to 4 hours (90mg)

OR 15minutes for ambulatory pump

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NOTE Selected Appendices ONLY
are in this pocketbook version- See
full version of the Systemic Therapy
Manual for Cancer Treatment for
ALL appendices

BODY SURFACE AREA

BODY SURFACE AREA (BSA)- ADULTS AND PEDIATRIC

$$\text{BSA (m}^2\text{)} = \frac{\text{kg}^{.725} \times \text{cm}^{.725}}{10.000} \times 71.84557$$

OR

$$\log \text{BSA (m}^2\text{)} = \frac{(\log \text{kg} \times 0.425) + (\log \text{cm} \times 0.725) + 1.8564}{10.000}$$

DuBois D and DuBois EF. "A Formula to Estimate the Approximate Surface Area if Height and Weight Be Known." *Arch Intern Med.* 1916 17:863-71

$$\text{BSA (m}^2\text{)} = \sqrt{\frac{\text{ht (in)} \times \text{wt (lb)}}{3131}}$$

OR

$$\text{BSA (m}^2\text{)} = \sqrt{\frac{\text{ht (cm)} \times \text{wt (Kg)}}{3600}}$$

Lam TK and Leung DT. "More on Simplified Calculation of Body-Surface Area." *N Engl J Med.* 1988; 318(17):1130 (letter)

Mosteller RD. "Simplified Calculation of Body Surface Area." *N Engl J Med.* 1987; 317:1098 (letter)

IDEAL BODY WEIGHT

Men: 50 kg + 2.3 kg/(inch >5 ft.)

Women: 45 kg + 2.3 kg/(inch >5 ft.)

Devine BJ. "Gentamicin Therapy." *Drug Intelligence and Clinical Pharmacy.* 1974; 8:650-5

OR

Men: 51.65 kg + 1.85 kg/(inch >5 ft.)

Women: 48.67 kg + 1.7 kg/(inch >5 ft.)

Robinson JD, Lupkiewicz SM, Palenik L, et al. "Determination of Ideal Body Weight for Drug Dosage Calculations." *Am J Hosp Pharm.* 1983; 40(6):1016-9

ADJUSTED BODY WEIGHT

Adjusted wt (kg) = actual weight (kg) - 0.4 [actual wt (kg) - ideal weight (kg)]

Notari EE. "Biopharmaceuticals and Clinical Pharmacokinetics." New York: Basel, 1987; 380

CREATININE CLEARANCE and AUC

In patients with stable renal function, the following formulas provide an acceptable estimate of the patient's creatinine clearance except in the following instances:

- Patient's serum creatinine is changing rapidly (either up or down).
- Patients are markedly emaciated.

In the above situations, certain assumptions have to be made.

- In patients with rapidly rising serum creatinine (ie, $>0.5-0.7$ mg/dL/day), it is best to assume the creatinine clearance is <10 mL/minute.
- In emaciated patients, although actual creatinine clearance is less than calculated creatinine clearance (due to decreased creatinine production), it is not possible to easily predict how much less.

Adults (18 years and older)

METHOD 1

(Cockcroft DW and Gault MH. *Nephron*. 1976; 16:31-41)

Estimated creatinine clearance (Cl_{cr}) (mL/min):

$$\text{Male} = \frac{(140 - \text{age}) \text{ IBW (kg)}}{72 \times S_{cr}}$$

$$\text{Female} = \text{estimated } Cl_{cr} \text{ male} \times 0.85$$

Note: The use of the patient's ideal body weight (IBW) is recommended for the above formula except when the patient's actual body weight is less than ideal. Use of the IBW is especially important in obese patients.

METHOD 2

(Jelliffe RW. *Ann Intern Med*. 1973; 79:604)

Estimated creatinine clearance (Cl_{cr}) (mL/min/1.73 m²):

$$\text{Male} = \frac{98 - 0.8 (\text{age} - 20)}{S_{cr}}$$

$$\text{Female} = \text{estimated } Cl_{cr} \text{ male} \times 0.90$$

Children (1-18 years)

METHOD 1

(Traub SL, Johnson CE. *Am J Hosp Pharm*. 1980; 37:195-201)

$$Cl_{cr} = \frac{0.48 \times (\text{height}) \times \text{BSA}}{S_{cr} \times 1.73}$$

where:

BSA = body surface area in m²

Cl_{cr} = creatinine clearance in mL/min

S_{cr} = serum creatinine in mg/dL

Height = in cm

AREA UNDER THE CURVE (AUC) FOR CARBOPLATIN DOSING

$$\text{Carboplatin (mg)} = \text{desired AUC} \times (25 + \text{GFR})$$

GFR = creatinine clearance (measured or estimated)

Calvert AH, Newell DR, Gumbrell LA, et al. "Carboplatin Dosage: Prospective Evaluation of a Simple Formula Based on Renal Function." *J Clin Oncol*. 1989; 7(11):1748-56

RENAL FUNCTION TESTS

ENDOGENOUS CREATININE CLEARANCE vs AGE

(Timed Collection)

Creatinine clearance (mL/min/1.73 m²) = $(Cr_u V / Cr_s T) (1.73/A)$

where:

Cr_u = urine creatinine concentration (mg/dL)

V = total urine collected during sampling period (mL)

Cr_s = serum creatinine concentration (mg/dL)

T = duration of sampling period (min) (24 h = 1440 min)

A = body surface area (m²)

Note: In patients with renal failure (creatinine clearance <25 mL/min), creatinine clearance may be elevated over GFR because of tubular secretion of creatinine.

CALCULATION OF CREATININE CLEARANCE

(From a 24-Hour urine collection)

Equation 1:

$$Cl_{cr} = \frac{(U) \times (V)}{P}$$

Cl_{cr} = creatinine clearance

U = urine concentration of creatinine

V = total urine volume in the collection

P = plasma creatinine concentration

Equation 2:

$$Cl_{cr} = \frac{(\text{total urine volume}) \times (\text{urine Cr concentration}) \times 100}{(\text{serum creatinine}) \times (\text{time of urine collection in minutes})}$$

Occasionally, a patient will have a 12- or 24-hour urine collection done for direct calculation of creatinine clearance. Although a urine collection for 24 hours is best, it is difficult to do since many urine collections occur for a much shorter period. A 24-hour urine collection is the desired duration of urine collection because the urine excretion of creatinine is diurnal and thus the measured creatinine clearance will vary throughout the day as the creatinine in the urine varies. When the urine collection is less than 24 hours, the total excreted creatinine will be affected by the time of the day during which the collection is performed. A 24-hour urine collection is sufficient to be able to accurately average the diurnal creatinine excretion variations. If a patient has 24 hours of urine collected for creatinine clearance, equation 1 can be used for calculating the creatinine clearance. To use equation 1 to calculate the creatinine clearance, it will be necessary to know the duration of urine collection, the urine collection volume, the urine creatinine concentration, and the serum creatinine value that reflects the urine collection period. In most cases, a serum creatinine concentration is drawn anytime during the day, but it is best to have the value drawn halfway through the collection period.

CANCER CHEMOTHERAPY AND CYTOTOXIC INJECTABLE DRUG DELIVERY STANDARDS- QEII HSC POLICIES



Queen Elizabeth II
Health Sciences Centre

September 1999

When physicians order cancer chemotherapy or cytotoxic drugs, it is necessary to indicate **ONLY** the drug, dose (per m² or kg), total dose, frequency and route of administration.

The Department of Pharmaceutical Services will prepare the intravenous (IV) medication in a standard fluid and volume to be administered at a specified rate according to the attached chart. A written order clarification will not be needed. The standardizations do not preclude the physician indicating other than standard fluid, volume or rate in cases which warrant such specifications (i.e. specific protocol). However in cases where a specific IV fluid is required for reasons of stability or compatibility, pharmacy will use the standard solution, and automatically clarify the order to the standard solution via a written clarification order.

CANCER CHEMOTHERAPY and CYTOTOXIC INJECTABLE DRUGS

IV Direct Administration Times: represent minimum times required

SVP: *Small Volume Parenteral* – a small volume parenteral consisting of ≤ 250 mL of IV solution generally inferring intermittent administration.

LVP: *Large Volume Parenteral* – a large volume parenteral consisting of ≥ 250 mL of IV solution generally inferring continuous administration.

APPENDIX 2A

Drug Name (Other Name)	Solution Volume		Administration Time
Asparaginase (Kidrolase ®)	D5W	SVP: 100 mL	30 minutes
Azathioprine (Imuran ®)		IV Direct Syringe (Physician Only)	Not less than 1 minute (Followed by 50 mL D5W or NS)
	D5W	SVP:	
		dose $\leq$ 100 mg = 50 mL	30 minutes
Bleomycin (Blenoxane ®)	NS	dose > 100 mg = 100 mL	30-60 minutes
	NS	SVP: 50 mL	15 minutes
	NS	Test Dose: 50 mL	15 minutes (prior to first treatment & wait 30 minutes)
Carboplatin (Paraplatin ®)	D5W	SVP: 250 mL	30 minutes
	D5W	LVP: 500 mL	2 hours (as per BMT protocol)
Carmustine (BiCNU ®)	D5W	SVP:	
		dose $\leq$ 500 mg = 250 mL	1 hour
Cisplatin (Platinol ®)	NS	dose > 500 mg = 250 mL	2 hours
	NS	SVP:	
	NS	dose < 30 mg/m ² = 250 mL	1 hour
Cladribine (2-CDA; Leustatin ®)	NS	LVP:	
	NS	dose $\geq$ 30 mg/m ² = 500 mL	2 hours
	NS	LVP: as per protocol	as per protocol over 24 hours
Cyclophosphamide (Procytox ®)	NS	LVP: 500 mL	2 hours
	BNS	LVP: 500 mL	2 hours
Cyclophosphamide (Procytox ®)	D5W	Continuous infusion	VIA ambulatory pump
	D5W	SVP: dose $\leq$ 500 mg/m ² = 100 mL	30 minutes
	D5W	dose > 500 - 1000 mg/m ² = 250 mL	1 hour
	D5W	LVP: dose > 1000 mg/m ² = 500 mL	2 hours
	NS	LVP: 250-1000 mL	as per protocol (BMT conditioning)
Cytarabine (ARA-C; Cytosar ®)	NS	LVP: 1000 mL	24 hours (as per protocol)
	D5W	SVP: 100 mL	
	D5W	(low dose) < 1 g/m ²	30 minutes
	D5W	LVP: doses > 1 g/m ² 250 mL-500 mL	$\geq$ 2 hours (as per protocol 2-3 hours)
	D5W	LVP: 1000 mL	24 hours (as per protocol)
	NS	Continuous infusion; intermittent infusion	VIA ambulatory pump

APPENDIX 2A

Dacarbazine (DTIC ®)	D5W	SVP: 250 mL	1 hour (or longer if painful)
Dactinomycin (Cosmegen ®)		IV Direct: Syringe	slowly over 1-5 minutes
Daunorubicin (Cerubidine ®)		IV Direct: Syringe	slowly over 1-5 minutes
Dexrazone (Zinecard ®)		SVP: Solution in an empty bag	15 minutes
Docetaxel (Taxotere ®)	D5W	SVP: 250 mL	60 minutes (or longer)
Doxorubicin (Adriamycin ®)		IV Direct: Syringe	slowly over at least 3-5 minutes
	NS	Continuous infusion (with vincristine)	VIA ambulatory pump
Epirubicin (Pharmorubicin ®)		IV Direct: Syringe	slowly over 3-5 minutes
Etoposide (VP-16; Vepesid ®)	D5W	LVP: dose $\leq$ 200 mg = 500 mL	60 minutes
		dose 201-235 mg = 600 mL	90 minutes
	D5W	LVP: maintain concentration $\leq$ 0.4 mg/mL	as per protocol
	NS	LVP: BMT conditioning	as per protocol
Fludarabine (Fludara ®)	D5W	SVP: 50 mL	30 minutes
5-Fluorouracil (5-FU, Adricil ®)		IV Direct: Syringe	over 1-2 minutes
		Continuous infusion	VIA ambulatory pump
	NS	LVP: 1000 mL	as per protocol
Ganciclovir (Cytovene ®)	D5W	SVP: 100 mL	1 hour
Gemcitabine (Gemzar®)	NS	SVP: 100 mL	30 minutes
Idarubicin (Idamycin ®)		IV Direct: Syringe	slowly over 3-5 minutes
Ifosfamide (Ifex ®)	D5W	SVP: dose $\leq$ 2000 mg = 250 mL	30 minutes
		LVP: dose > 2000 mg = 500 mL	1 hour
Interferon-Alfa-2b (Intron A ®)	NS	SVP: 100 mL	20-30 minutes
Irinotecan (CPT-11; Camptosar ®)	D5W	LVP: 500 mL	90 minutes
Mechlorethamine (Nitrogen Mustard; Mustargen ®)		IV Direct: Syringe	slowly over 1- 5 minutes
Melphalan (Alkeran ®)	NS	SVP: 100 mL	15 minutes

APPENDIX 2A

Methotrexate (MTX)		IV Direct: low doses ≤ 40 mg/m ² syringe	over 1-2 minutes
	D5W	SVP: dose 100 - 200 mg = 100 mL	20 minutes
	D5W	dose 201 mg-500 mg = 250 mL	30 minutes
	D5W	LVP: dose 501 - 1000 mg = 500 mL	1 hour
	D5W	LVP: high dose	as per protocol
Mitomycin (Mutamycin ®)		IV Direct: Syringe	slowly over 2-5 minutes
Mitoxantrone (Novantrone ®)		IV Direct: Syringe	slowly over 3-5 minutes
Paclitaxel (Taxol ®)	D5W	LVP: 500 mL	3 hours
Raltitrexed (Tomudex ®)	D5W	SVP: 50 mL	15 minutes
Rituximab (Rituxan ®)	D5W	SVP: final concentration of 1-4 mg/mL (as per protocol)	<u>First Infusion:</u> 50 mg/hour escalate 50 mg/hour increments q30 minutes if tolerated to max of 400 mg/hour <u>Subsequent Infusion:</u> 100 mg/hour escalate rate 100 mg/hour increments q30 minutes if tolerated to max of 400 mg/hour
Streptozocin (Zanosar ®)	D5W	SVP: 100 mL	30 minutes
Thiotepa		IV Direct: Syringe	IV push over < 1 minute
Topotecan (Hycamptin ®)	D5W	SVP: 50 mL	30 minutes
Trastuzumab (Herceptin ®)	NS	SVP: 250 mL	90 minutes loading dose 30 minutes maintenance dose
Vinblastine (Velbe ®)		IV Direct: Syringe	over 1 minute
Vincristine (Oncovin ®)	NS	IV Direct: Syringe Continuous infusion (with doxorubicin)	over 1 minute VIA ambulatory pump
Vinorelbine (Navelbine ®)	NS	IV Direct: Syringe	over 6-10 minutes

GUIDELINES FOR THE MANAGEMENT OF EXTRAVASATION OF CANCER CHEMOTHERAPY AGENTS- QEII HSC POLICIES

Prepared by: Pharmacy Department in Conjunction with Oncology/
Medical Surgical Specialities/ Transplant Nursing
Date Approved by Oncology Therapy Subcommittee: May 23, 1997

I. DEFINITIONS

Infiltration: Refers to the (IV) intravenous cannula which has slipped from a vein into the tissue.

Extravasation: Misdirection of intravenous fluid or medication from a blood vessel into interstitial tissue.

Vesicant: An agent capable of causing tissue necrosis when infiltrated from the vein into the subcutaneous tissue causing progressive severe tissue damage.

Irritant: An agent capable of causing pain and local inflammation but not tissue necrosis.

Venous flare: A local phenomena characterized by infrequent local edema, venous streaking and pruritus along the vein which does not result in tissue damage. This reaction is demonstrated by such agents as doxorubicin, daunorubicin, epirubicin, idarubicin and mechlorethamine and appears to be a local hypersensitivity or inflammatory reaction.

II. CLINICAL DIFFERENCES BETWEEN FLARE REACTIONS AND EXTRAVASATION

VENOUS FLARE REACTION

- dull ache
- erythema
 - proximal along vein
 - tiny papules or itching (pruritis) around point of entry
- edema
 - none or infrequent at the IV site and good blood return is still obtained
- reaction usually resolves in 30-45 min.
- the immediate redness (raised red streak) and swelling can occur resolving quickly and rarely lasts longer than 12-24 hrs.

EXTRAVASATION

- pain, burning, stinging
- erythema
 - seen at site of injection
- edema
 - Is common, redness, blanching and blistering at injection site, some injuries may occur away from injection site
 - blood return may or may not be present (blood return may be absent or sluggish)(blood return may be present i.e. damaged vein - rupture, leak from a damaged vessel; needle may have punctured the wall of the vein leaving a greater portion of the bevel within the lumen of the vein

III. SIGNS AND SYMPTOMS OF A CANCER CHEMOTHERAPY EXTRAVASATION

(Vesicant/Irritant Drugs - see individual agents in sections IV & V)

PAIN	Pain, stinging or burning at injection site May last minutes or hours and eventually subsides
ERYTHEMA	At injection site or along a weakened blood vessel May not always be present at time of extravasation and may occur later
SWELLING	Can be severe and usually occurs immediately Loss of IV backflow (backflow may be present, but sluggish); lack of blood return when checking the IV line
ULCERATION (tissue necrosis)	Usually occurs 48-96 hours later If partial skin thickness is damaged the area may appear as a blister If full thickness of skin is damaged, the surface may appear very white and develop an eschar (a slough) Injury can progress with the formation of deep necrotic lesions and can continue to occur for months

**IV. LIST OF VESICANT CANCER CHEMOTHERAPY DRUGS AVAILABLE
ON THE QEII HEALTH SCIENCES CENTRE FORMULARY**

CANCER CHEMOTHERAPY VESICANTS

Generic Name	CLINICAL COMMENT ON EFFECTS OF EXTRAVASATION
Dactinomycin	• immediate pain, erythema, swelling • known to produce severe skin ulcers
Daunorubicin	• Immediate pain, erythema and swelling • severe skin ulcers
Doxorubicin	• immediate pain, erythema and swelling • severe progressive tissue necrosis • blisters may appear in 1-2 days and ulceration days to weeks after extravasation
Epirubicin	• same as doxorubicin
Idarubicin	• same as doxorubicin
Mechlorethamine (Nitrogen Mustard)	• immediate pain and swelling • severe and prolonged skin ulcers; lesions heal poorly
Mitomycin-C	• initial local erythema, edema, and pain • progress slowly to non-healing skin ulcerations • symptoms are sometimes delayed months; lesions can expand over weeks
Streptozocin	• tissue necrosis • burning sensation at injection site and up the arm
Vinblastine	• produces pain, erythema and localized swelling within minutes • skin blisters form after several days and resolve slowly over several weeks
Vincristine	• same as vinblastine
Vinorelbine	• produces pain, erythema, localized swelling • local tissue necrosis and/or thrombophlebitis • venous discoloration • possible ulceration

**V. LIST OF IRRITANT CANCER CHEMOTHERAPY DRUGS ON THE QEII
HEALTH SCIENCES CENTRE FORMULARY**

CANCER CHEMOTHERAPY IRRITANTS

Generic Name	CLINICAL COMMENT ON EFFECTS OF EXTRAVASATION
Carmustine	• possible phlebitis due to ethanol content (drug reconstituted with ethanol)
Cisplatin	• rarely produces necrosis and only when large amount of highly concentrated solution is extravasated
Dacarbazine	• phlebitis is rare • light induced activation pathway of drug suggests protection of exposed tissues from light during administration
Docetaxel	• localized pain and discoloration of skin • erythema, desquamation
Etoposide	• phlebitis, urticaria and erythema (due to drug formulation) • possible skin ulceration
Mitoxantrone	• does not appear to consistently produce necrosis if extravasated • relatively painless upon immediate extravasation • blue discoloration of skin • possible ulceration
Paclitaxel	• Inflammation • pain, erythema, cellulites • possible sclerosis, hyperpigmentation, skin ulceration and peeling and blistering of skin

VI. FACTORS INCREASING THE RISK OF EXTRAVASATION**1. Type of Drug Infused**

Refer to sections IV and V - Lists of vesicant or irritant cancer chemotherapy agents

Drug-Related Risk Factors

- a) Vesicant potential of drug
- b) Drug concentration and volume extravasated
- c) Drug vehicle - solvents used to allow the drug to remain in solution
- d) Order of administration - Although a very controversial subject, vesicants are to be administered first at the QEII Health Sciences Centre.
- e) Inadequate flushing of the line before and after each drug.

2. General Considerations

- a) Anatomical disruptions that may interfere with venous flow.
- b) Alterations in mental status caused by i.e. sedation, antiemetics.
Confusion caused by such drugs may cause inability to communicate discomfort.
- c) Sudden movements due to emesis or urgency to void.
- d) Patients condition - previous cancer chemotherapy treatment degree of debilitation.
- e) Peripheral neuropathy i.e. unable to feel pain
- f) Patient may be obese or dehydrated thereby making it difficult to identify swelling or hardness.
- g) Irradiated limbs, areas distal to lymphatic blockage or areas close to recent venipuncture.

3. Peripheral Route

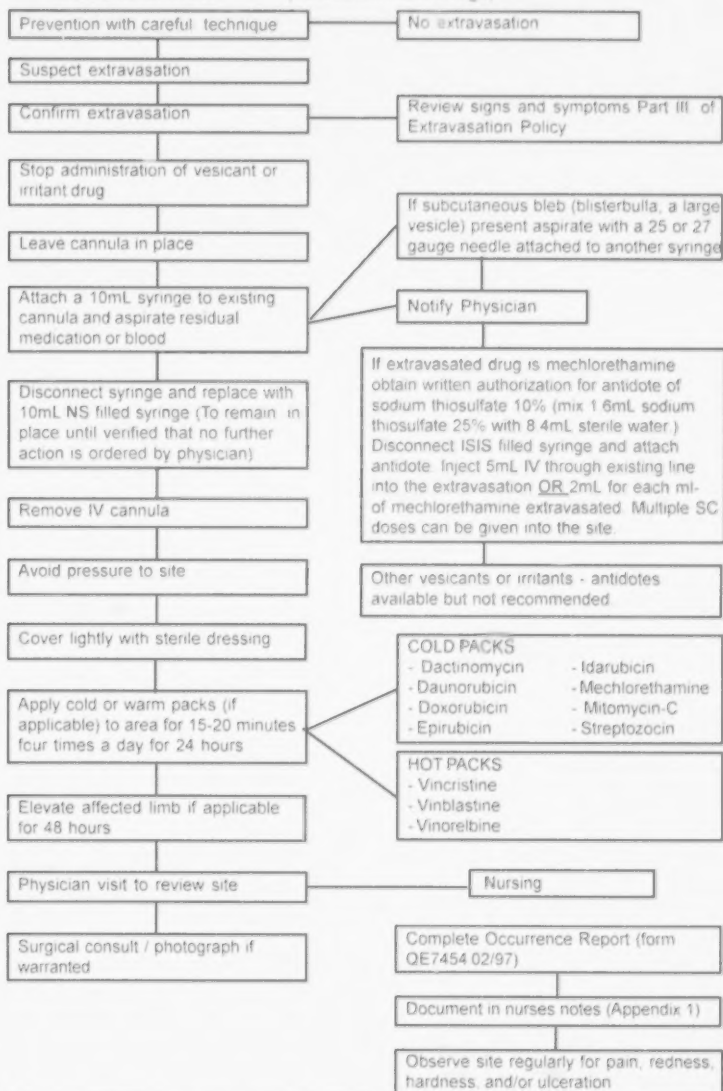
- a) Inappropriate site for venipuncture i.e. puncturing a vein more than once.
- b) Previous vascular trauma
- c) Dislodgement of needle
- d) Infusion sites distal to obstructed venous drainage
- e) Poor blood return
- f) Increased length of infusion times i.e. continuous infusion
- g) Old vein (either vein on elderly person or use of a long standing IV site > 24 hours)

4. Central Route

- a) Poor blood return (sluggish or absent)
- b) Improper and insecure Huber needle placement in the port of an implanted infusion port
- c) Occluded catheter (partial or complete)
- d) Internal catheter being disconnected from port
- e) Improper position of catheter

APPENDIX 2B

VII. ALGORITHM FOR MANAGING CANCER CHEMOTHERAPY EXTRAVASATION (Vesicant/Irritant Drugs)



APPENDIX I

Documentation of information on Nurses' notes in patient's medical record

1. Date
2. Time
3. Type of venous access (i.e. needle size, peripheral route, right atrial catheter, implanted port)
4. Insertion site, location (appearance)
5. Number of venipuncture attempts and location
6. Drug sequence of non-chemotherapy and chemotherapy drugs given immediately prior to extravasation
7. Drug(s) that extravasated
8. Drug administration techniques, small volume parenteral (SVP), large volume parenteral (LVP), push
9. Estimated amount of drug extravasated
10. Symptoms reported by patient and patient's response
11. Nursing intervention
12. Appearance of site
13. Physician notified
14. Plastic surgery consult / photograph (if warranted)
15. Follow-up instructions to patient
16. Nurse's signature

GUIDELINES FOR THE MANAGEMENT OF HYPERSENSITIVITY REACTIONS/ANAPHYLAXIS WITH CANCER CHEMOTHERAPY AGENTS- QEII HSC POLICIES

Anaphylaxis

- Syndrome elicited in a hypersensitive individual on subsequent exposure to a sensitizing antigen
- Ranges from localized response to systemic response which may lead to anaphylactic shock and death

Hypersensitivity Drug Reactions

<i>Allergic Drug Reactions</i>	<i>Mechanism of Action</i>	<i>Examples</i>
Type 1	Re-exposure to a particular antigen/IgE mediated (immediate reaction)	Penicillin allergy; most chemotherapeutic agents
Type 2	Cytotoxic reactions Manifest as hemolytic anemia, thrombocytopenia and granulocytopenia	Transfusion reactions
Type 3	Immune complex-mediated reactions	Systemic lupus erythematosus; serum sickness
Type 4	Cell-mediated (delayed reactions)	Graft rejection; contact dermatitis

Cancer Chemotherapy Agents

Most cancer chemotherapy agents can produce hypersensitivity reactions. Type 1 is the most common reaction documented. Type 1 hypersensitivity reactions occur when an antigen interacts with IgE bound to a mast cell membrane causing degranulation of mast cells.

Anaphylactoid Drug Reactions

Do **NOT** involve immunologic mediators. May occur upon first exposure - NOT IgE mediated

Discussion

- May have no correlation with the known pharmacologic properties of the drug
- May occur on first exposure or develop after subsequent administration (i.e. a number of previous cycles)
- Only occurs in a small percentage of patients
- May present with early or late onset of symptoms
- Chemotherapeutic agents for which pre-medications are routinely used to prevent adverse reactions
 - docetaxel
 - paclitaxel
 - rituximab
 - trastuzumab
 - monoclonal antibodies (in general)

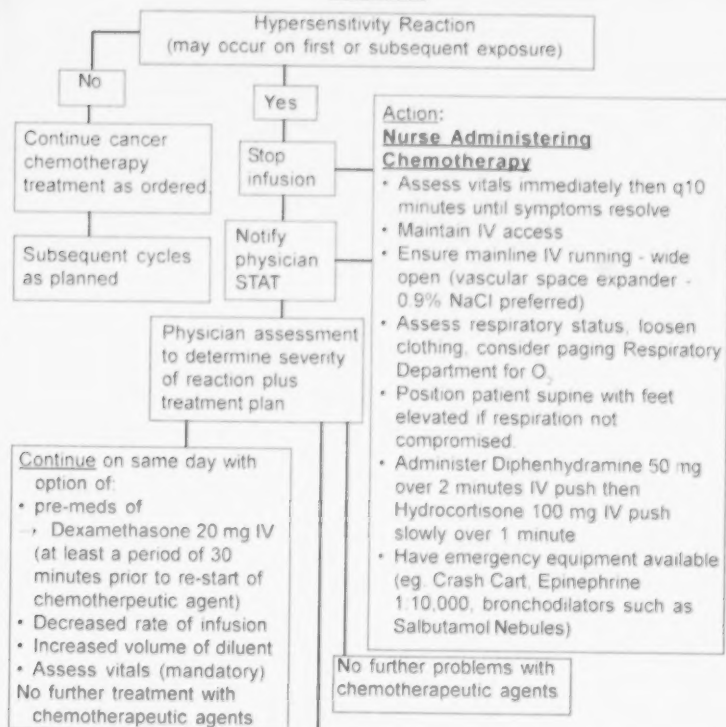
- Chemotherapeutic agents for which pre-medications are not routinely used but which may require treatment for allergic reactions that can occur during infusion
 - carboplatin
 - etoposide
- The patient should be closely monitored when receiving drugs with documented potential for hypersensitivity response. The Registered Nurse (RN) must remain with the patient for the first 15 minutes when administering these drugs. Most reactions become evident early on within seconds or minutes after exposure to an antigen.

Recognition and Clinical Features

Cutaneous	facial flushing; urticaria rash; hives; pruritis; angioedema
Cardiovascular	pain; headache; chills; tachycardia; hypotension; hypertension; arrhythmias; shock; syncope
Gastrointestinal	abdominal bloating; cramps; vomiting; diarrhea
Respiratory	dyspnea; bronchospasm; laryngeal spasm; wheezing; chest tightness; rhinorrhea; nasal congestion
Others	agitation; back pain; diaphoresis; fecal or urinary incontinence; anxiety; feeling of impending doom; "just don't feel right"

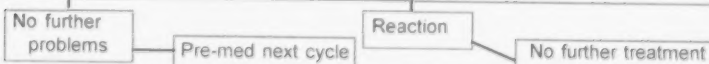
APPENDIX 2C

Algorithm



Rechallenge at a later date after option of:

- pre-meds of
 - Dexamethasone 20 mg IV or oral dexamethasone 20 mg po 6 and 12 hours pre (i.e. Taxol) [at least a period of 30 minutes prior to start of chemotherapeutic agent]
 - Diphenhydramine 50 mg IV [at least a period of 30 minutes prior to start of chemotherapeutic agent]
 - Ranitidine 50 mg IV [at least a period of 30 minutes prior to start of chemotherapeutic agent]
- Decreased rate of infusion
- Increased volume of diluent
- Have emergency equipment available (eg. Crash Cart, Epinephrine 1:10,000, bronchodilator such as Salbutamol Nebules)



Retreatment Discussion

- Careful consideration of the risk versus benefit
- Discussion between patient and physician
- May be successful in certain circumstances: interventions with pre-medications such as H₁ and H₂ antagonists and/or a variety of options including increasing fluid volumes or slowing infusion rates may allow for re-treatment
- Most frequent agents encountered are listed below

<u>Chemotherapeutic Agent</u>	<u>Patients at Greatest Risk of Hypersensitivity Reaction</u>	<u>Re-Treatment Possibilities</u>
Taxanes* (Paclitaxel or Docetaxel)	Patients receiving 1 st or 2 nd dose	Yes, in virtually all patients
Platinum Compounds* (Carboplatin or Cisplatin)	Patients receiving multiple (>6) courses	Occasionally
Epipodophyllotoxins* (Etoposide or Teniposide)	Patients receiving multiple courses. Reactions with the first exposure may occur.	Very little data in the literature
Asparaginases* (Escherichia coli asparaginase, Erwinia asparaginase)	Patients receiving multiple courses; patients receiving re-induction chemotherapy	Possibility
Rituximab	Patients receiving 1 st dose. Patients with a high number (>25,000/mm ³) of circulating malignant cells or high tumour-burden	Yes
Trastuzumab	Symptoms generally occur during an infusion but onset may be after completion of an infusion. Patients with symptomatic intrinsic lung disease or with extensive tumour involvement of the lungs resulting in dyspnea at rest, may be at greatest risk of severe reactions.	Yes

* Adapted from Prevention and Management of antineoplastic-induced hypersensitivity reactions. Drug Safety 2001; 24 (10): 776 (Table VII)

Systemic Therapy Program

Policies & Procedures

ORDERING CANCER CHEMOTHERAPY**GUIDING PRINCIPLES**

Cytotoxic chemotherapy for cancer patients is a high-risk area of pharmacotherapy. Specific policies and procedures are needed to ensure quality patient care, including safe ordering and administration of drugs. When a chemotherapy regimen will be appropriately offered at a local facility, clear policies and procedures are needed to outline how the care and treatment information is transferred between facilities and staff, without miscommunication. Each treatment facility will have policies that define roles, responsibilities, and functions to minimize the risk of error in the ordering and delivery of chemotherapy. Quality care and safety must be considered when orders are generated for administration either at the same facility or elsewhere.

Oral chemotherapy agents, generally given by patient self-administration are not filled by the hospital pharmacy nor administered by hospital nursing staff. However, these drugs may be hazardous to patients if taken incorrectly. The policies and procedures consider the ordering of oral chemotherapy agents, in order to reduce the potential for dispensing or administration error.

In Nova Scotia, cytotoxic chemotherapy may be ordered for local administration in either a Cancer Care Program facility, or an outreach facility, or recommended by an oncologist for administration at another facility, or by another specialist at the local facility. These policies and procedures are designed to address any of these possibilities. Policies and procedures, common to all health districts in Nova Scotia, will enhance clarity and relationships between health care professionals providing chemotherapy care, and thus further improve patient safety and quality care.

Cancer Care Nova Scotia (CCNS) is the provincial cancer program, with a mandate to develop standards of cancer care across Nova Scotia. CCNS has assisted, through development of District Cancer Programs, overseen by District Cancer Committees. To support safe, accessible and efficient delivery of systemic therapy, the District Cancer Programs and CCNS are in the process of developing an integrated model for cancer care. This includes determining which cytotoxic chemotherapy regimens are appropriate for safe delivery at different facilities, based upon resources, staffing and local expertise. This 'Levels of Care' model will guide District Health Authorities on specific decisions to offer local care or to defer care to another facility. Programs to improve knowledge and education of health professionals in the care of cancer patients are under development, and will be an integral component of the competency development needed to fulfill this package of policies and procedures. CCNS has developed a "Systemic Therapy Manual for Cancer Patients", cataloging appropriate levels for each regimen and to provide information support to all health care professionals involved with cancer patients.

Chemotherapy ordering and administration is more complex than ordering many other drugs in the hospital setting due to risk and safety concerns. There is considerable support to restrict the ordering of these dangerous drugs to physicians, who have a high level of cancer-specific training.

It is the purpose of these Policies and Procedures, the underlying 'Levels of Care' structure, and tools developed by CCNS (such as the preprinted Physician Standing Orders), to ensure the safety of patients receiving cancer chemotherapy, and to facilitate local access to this service. The policies and procedures are intended to become a capacity building tool to enhance both safety and communications between treatment facilities and districts.

DEFINITIONS

1. *Cancer Chemotherapy*: A single drug or combination of drugs used for the treatment of cancer. The cancer chemotherapy drugs may or may not be cytotoxic. Additional drugs may be added as Supportive Treatment to help ameliorate adverse effects of the cancer treatment or the disease. This does not include hormone agents.
2. *Systemic Therapy*: The use of drugs for the treatment or support of cancer patients. Systemic therapy includes cancer chemotherapy, hormone therapy, immunotherapy and supportive care drugs, and includes drugs given by any route, including oral.
3. *Parenteral*: A drug administered to a patient by a route other than enteral (via the gut). This may include intravenous, subcutaneous, intramuscular, intradermal, intrathecal, intravesicular, or intrahepatic. Since the integumental barrier will be breached in administration, precaution is required to ensure the product is aseptic.
4. *Cancer Chemotherapy Regimen*: The combination of chemotherapy drug or drugs, with predetermined relative or absolute doses, schedule of administration, and often with recommended supportive therapy (e.g. antiemetics, hydration).
5. *Cancer Chemotherapy Cycle*: A drug or combination of drugs, which is given to a patient over a fixed period of time or within a defined interval. Usually the cycle of cancer chemotherapy agent(s) will repeat at the start of the next time period. Most cancer chemotherapy regimens are given in repetitive cycles. Some cancer chemotherapy regimens include cycles with a different drug or combination of drugs planned for the next time period. The duration of a cycle is generally 2 to 8 weeks, and may be followed by the subsequent pre-determined cycle.
6. *Cancer Chemotherapy Protocol*: The full number of cycles of cancer chemotherapy from beginning to end of the planned treatment. Alterations in the drugs (such as dose reductions or delays), to accommodate toxicities or events during the protocol, do not indicate the protocol is ended, but a decision to change the cancer chemotherapy regimen indicates the end of one protocol course and the beginning of another.

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7. *Cancer Care Program*: Program of combined cancer care services in Capital Health for adults (or Cape Breton Health Science Centre for adults or IWK Health Centre for children and adolescents). The Cancer Care Program in Capital Health includes inpatient and outpatient operating units, and includes health professionals or other supports managed by other departments (e.g. pharmacy, social work, psychology) or physicians (managed by departments of Dalhousie University).
8. *District Cancer Program*: District Cancer Programs (DCP) are structures that will deliver the integrated, coordinated cancer services based on patient needs and safety. Underlying the concept of the DCP is the awareness of the fragmentation that currently exists in cancer care. A wide range of health professionals and volunteers working for a variety of organizations within a District (although not necessarily within the mandate of the District Health Authority) are caring for patients with cancer. There is often duplication of services as well as gaps. Because there are few provincial standards, services are often provided in different ways.
9. *District Cancer Committee*: The District Cancer Committee will bring together all those in a District with an interest in cancer care to work towards common goals for integrated cancer care within the District.
10. *Outreach Oncology Program*: Program in regional hospital for cancer care, which includes regular visits by an oncologist. The oncologist may assess cancer patients and order chemotherapy appropriate to the level of chemotherapy delivery for that hospital.
11. *Chemotherapy Administration Unit*: A facility (usually hospital) unit dedicated for the local preparation and delivery of chemotherapy. A Chemotherapy Administration Unit requires a dedicated space for cancer patient drug administration (sometimes called a chemotherapy suite), a dedicated drug preparation area (which may be located in the hospital pharmacy department), dedicated oncology nursing staff (which includes at least one Registered Nurse with Chemotherapy Certification), and on-site medical supervision (by a Community Physician with Chemotherapy Privileges or a Community Physician with Oncology Privileges). *For treatment of pediatric cancer patients, there should be a properly equipped, dedicated space within the Chemotherapy Administration Unit for administration of chemotherapy to a child, a Registered Nurse with Chemotherapy Certification and pediatric experience, and a pediatrician as the physician with prescribing privileges.* It is desirable that a Chemotherapy Administration Unit has access to a hospital pharmacist with oncology training.
12. *Levels of Care for Cancer Chemotherapy*: A program to determine the resources [health professionals, services and facilities] needed to safely administer each chemotherapy agent or combination of agents. The Levels of Care system and designations for systemic chemotherapy are under development by Cancer Care Nova Scotia (CCNS), and, for pediatric oncology, CCNS in collaboration with the Atlantic Provinces Pediatric Hematology Oncology Network (APPHON). The service components will include the required degree of expertise for all health care professionals

APPENDIX 2D

involved in delivery of care to adults or children with cancer, availability of other hospital services and other factors related to patient safety during chemotherapy administration. Chemotherapy regimens will also be categorized [as basic, intermediate, advanced, or sub-specialty] to determine the health care facility in which the regimen may safely be administered. For some protocols, portions of the entire protocol may be categorized with different levels, allowing for transfer of some of the chemotherapy treatments. Chemotherapy care will not be transferred to a health care facility without the resources in place to deliver that regimen

13. *Oncologist*: A physician with specialized training in the management of cancer. Specialization may be formal or informal, and may be subcategorized within other specialty disciplines (e.g. gynecology, pediatrics, hematology, urology, thoracic surgery, etc.) or specific to cancer (e.g. medical oncology, radiation oncology). A physician designated as an *Oncologist* will be granted privileges for the full practice of cancer care within the scope of their specialty practice area and/or time limitation for cancer care.
14. *Pediatric Oncologist*: A pediatrician with specialized training in the management of childhood cancer.
15. *Oncologist Delegate*: A physician in training (e.g. resident, fellow) or a Clinical Associate, under the supervision of an oncologist. The Oncologist Delegate may perform the duties of an oncologist while under supervision, and may be included when Oncologist roles are mentioned in these policies and procedures.
16. *Community Physician*: A community physician, with accredited prescribing privileges in the local treatment facility, designated to supervise a cancer patient through local cancer chemotherapy treatments. *This physician may be a pediatrician for the local treatment of children with cancer.* This physician has privileges to order cancer chemotherapy, which has been recommended on consultation by an Oncologist, a *Pediatric Oncologist*, or a Community Specialist. For treatments given at the local treatment facility, this physician might be referred to as the 'most responsible physician'.
17. *Community Specialist*: A community specialist physician, with accredited prescribing privileges in the local treatment facility, designated to assess and diagnose cancer patients, and to initiate a cancer chemotherapy program within a defined scope of practice, as defined by the District Health Authority in consultation with *Cancer Care Nova Scotia*. For treatments given at the local treatment facility, this physician might be referred to as the 'most responsible physician'.
18. *Oncology Nurse*: A nurse who is experienced and skilled in the care of cancer patients and their families.
19. *Registered Nurse with Chemotherapy Certification*: The administration of cancer chemotherapy is a shared competency and requires that a Registered Nurse complete a specified training program. The oncology nurse with chemotherapy certification will hold a current certificate from the training program, and will be responsible for maintenance of certification, as

APPENDIX 2D

defined by the health district (in collaboration with *Cancer Care Nova Scotia*). For privileges to administer chemotherapy to a pediatric oncology patient, this nurse will also have pediatric experience or work closely with a pediatric nurse (in this case certification may also be in collaboration with the IWK Health Centre/APPHON).

20. *Family Care Coordinator*: A registered nurse responsible for coordinating the shared care of childhood cancer patients from home to pediatric tertiary centre to home.
21. *Oncology Pharmacist*: A pharmacist, trained and assigned to a clinical practice in the Cancer Care Program by the Pharmacy Department. An oncology pharmacist is certified through a training program offered in consultation with *Cancer Care Nova Scotia* or an equivalent pediatric program.
22. *Hospital Pharmacist with Oncology Training*: A hospital pharmacist, with oncology-specific training, competency assessment and practice privileges in the local treatment facility, designated to verify cancer chemotherapy treatment orders within a scope of practice, defined by the District Health Authority in consultation with *Cancer Care Nova Scotia*. For privileges to verify chemotherapy for a pediatric oncology patient, this pharmacist may also have pediatric oncology specialty training (in collaboration with the IWK Health Centre/APPHON).
23. *Health Record*: The health record that contains the health information related to the cancer diagnosis of a patient. When referred to as the "relevant health record", the record must include all information related to diagnosis, staging, and all other information needed for the decision to treat the patient with cancer. When referred to as the "current health record", the record must include the relevant health information related to the current chemotherapy protocol needed for the clinical decision to continue with the current treatment. Prescribers ordering chemotherapy treatments are responsible for ensuring that all necessary medical information is available (including the current consultant letter, when care is transferred), prior to ordering these drugs.
24. *Pre-Printed Order (PPO) Form*: A preprinted order sheet, approved by the appropriate Cancer Site Team, and the Capital Health Forms Committee (for format). For pediatric oncology, the chemotherapy order forms approved by APPHON and IWK will be considered as PSO for this document.
25. *Generic Pre-Printed Order (PPO-G) Form*: A form designed with the same format as an approved Physician Standing Order, including key criteria for monitoring and actioning items, for ordering cancer chemotherapy regimens not preprinted and approved on a Physician Standing Order.
26. *Pre-Printed Order for Oral Chemotherapy (PPO-O) Form*: A preprinted order sheet, approved by the appropriate Cancer Site Team, and the Capital Health Forms Committee (for format), and intended for the ordering of oral chemotherapy drugs to be dispensed by the patient's community pharmacy.

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27. *Systemic Therapy Manual for Cancer Treatment*: A manual listing all drugs and treatment regimens typically used within Nova Scotia. The *Systemic Therapy Manual* is published and updated by the Systemic Therapy Program of Cancer Care Nova Scotia.
28. *Provincial Cancer Drug Formulary*: A listing of drugs used in cancer care, with the formulary status of each drug according to the Levels of Care Systemic Therapy Criteria. Drugs are listed as available or restricted appropriate to each facility level. DHAs will be recommended to adopt a standard formulary for cancer drugs across Nova Scotia.
29. *Roadmap*: The treatment protocol document for pediatric cancers that outlines the treatment and monitoring for each phase of each specific treatment protocol.

POLICIES

1. All health care professionals involved with cancer chemotherapy will hold privileges or be certified by the appropriate authorities.
2. It is the responsibility of the health care professionals involved with cancer patient care to ensure that no order for systemic therapy, to be administered at another facility or to be self-administered by the patient, will be transmitted to the other facility or given to the patient or family until all quality checks are completed
 - a. Any facility where the systemic therapy is to be administered is responsible for completion of quality checks before any dose of chemotherapy is administered.
3. If cancer chemotherapy administration is transferred to another facility, a local physician (either a *Community Physician* or a *Community Specialist*) must agree to supervise the patient while receiving chemotherapy and to be responsible for patient care while at the local facility.
4. All patients receiving cancer chemotherapy will be assessed by an *Oncologist* or *Community Specialist* prior to initiation of a cancer chemotherapy protocol.
5. Each patient will be assessed within 1 week prior to the start of each cycle. Assessment will be a shared responsibility among the *Oncologist*, *Oncologist Delegate*, *Community Specialist*, *Oncology Nurse*, *Registered Nurse with Chemotherapy Certification*, and *Oncology Pharmacist* (or *Hospital Pharmacist with Oncology Training*).
6. If the care has been transferred to another facility, assessment will be a shared responsibility among the *Community Physician*, the *Oncology Nurse* (or *Registered Nurse with Chemotherapy Certification*), and the *Hospital Pharmacist with Oncology Training* at the local site.
7. Each patient receiving cancer chemotherapy treatment should have a plan for ongoing monitoring over the full duration of the treatment protocol.
8. The treatment care and monitoring plan will be available to all health care professionals involved with the patient's care. Local physicians and other health care professionals should document changes within the plan.

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9. Prior to administration of the first dose of a cancer chemotherapy protocol (including oral cancer chemotherapy), each patient will sign an informed consent for chemotherapy according to institutional policy.
10. All orders for cancer chemotherapy will be written and signed by an *Oncologist* or *Community Specialist* and closely supervised by an *Oncologist* for physicians-in-training.
 - a. The initial cycle of chemotherapy must be countersigned by an *Oncologist* for physicians-in-training.
 - b. Intrathecal chemotherapy will only be ordered and administered in a facility with an approved policy for this procedure.
 - c. Specialized chemotherapy procedures (e.g. intra-vesicular bladder instillations, pleurodesis, intra-hepatic or intra-arterial infusions may be administered by other specialists, such as surgeons, internists, gastroenterologists or radiologists), only according to specific policies & procedures approved by the district health authority.
11. The *Oncologist* or *Community Specialist* will use the available & approved *Pre-Printed Order* (PPO) or *Pre-Printed Order for Oral Chemotherapy* (PPO-O), for a written order of each cycle of cancer chemotherapy (including inpatients, ambulatory care patients and take-home prescriptions).
 - a. A *Pre-Printed Order* is only valid for a single cycle of cancer chemotherapy, unless it has been formatted and approved for multiple cycles of chemotherapy.
 - b. The ordering *Oncologist* or *Community Specialist* will not order more cycles of chemotherapy than are included in the approved format of the PPO.
 - c. The ordering *Oncologist* or *Community Specialist* will ensure that the correct PPO form is used for each patient, including correct regimen and correct diagnosis (where similar regimens exist for different diagnoses or stages)
 - d. The *Oncologist* or *Community Specialist* will ensure that the PPO is fully completed, appropriate to the specific regimen and cycle, if appropriate.
 - e. If no preprinted PPO is available for the cycle of cancer chemotherapy, a *Generic Pre-Printed Order* (PPO-G) *Form* should be used, particularly if chemotherapy is to be administered by a route other than intravenous (e.g. intra-operative, or administered by instillation into the bladder).
 - f. If an oral chemotherapy agent is part of the chemotherapy regimen, the prescriber will use the appropriate *Pre-Printed Order for Oral Chemotherapy* (PPO-O) *Form*.
 - i) If there is no preprinted PPO-O, the *Oncologist* or *Community Specialist* is responsible to ensure that the mandatory information included on a PPO-O is included on the patient take-home prescription.
 - g. Chemotherapy must be ordered according to the stipulations of the preprinted PPO or PPO-O.
 - i) No chemotherapy drug may be added or substituted to a PPO or PPO-O.

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- ii) A chemotherapy drug may be deleted from the PSO, with a clinical explanation written on the PPO or PPO-O.
 - iii) The administration route of any chemotherapy drug will not be changed on the PPO or PPO-O.
 - iv) The dose of any chemotherapy drug will not be increased above the identified relative dose (e.g. mg/m², AUC).
 - v) The dose of any chemotherapy drug may be decreased below the identified relative dose (e.g. mg/m², AUC) or the total dose may be decreased (e.g. removal of one or more days), with a clinical explanation written on the PPO or PPO-O.
 - vi) Although the dosing frequency may be adjusted within 1-2 days to accommodate for holidays, weekends, or other necessary calendar adjustments, frequency or dose will not otherwise be increased.
 - vii) Any decrease in dosing frequency will be documented on the PPO or PPO-O with a clinical explanation.
12. If it is necessary to change or delete part of the chemotherapy orders, that portion must be cancelled on the PPO or PPO-O and a new order will be written for the balance of the cycle or course.
 - a. If a portion of the PPO is cancelled part way through the cycle, the cancelled portion (i.e. drugs and/or dosages) of that PPO will be stroked out and marked as void with the void date and prescriber signature.
 - b. A new physician order will be written to clarify the order change.
 - c. If a PPO is formatted for multiple cycles of chemotherapy or multiple visits within a cycle, a new PPO is required for any changes to the chemotherapy part way through the cycle(s).
13. If cancer chemotherapy administration is transferred to another facility, the *Oncologist* or *Community Specialist* will complete a PPO or a PPO-G form, as required for treatments given at the Cancer Care Program facility.
 - a. The *Oncologist* or *Community Specialist* may recommend a specific number of cycles of chemotherapy to be given at the local facility, or an entire chemotherapy protocol. The number of cycles must be specified on the PPO or PPO(G) transmitted to the local facility and documented in the treatment plan.
 - b. A PPO or PPO-G is only valid for a single cycle of cancer chemotherapy when transferred to another facility for administration. All subsequent cycles, which are ordered locally, must be written for single cycles only.
 - c. If multiple cycles (or the entire chemotherapy protocol) were recommended by to be given at the local facility, the local physician responsible for the chemotherapy treatment will use the correct PPO to order each subsequent cycle (one cycle at a time).
 - d. The local physician may only make changes to the PPO in consultation with the *Oncologist* or *Community Specialist*.
 - e. Prior to transmission of the cancer chemotherapy PPO to another facility, the order will be verified and countersigned by both an *Oncology Nurse* (or *Registered Nurse with Chemotherapy*

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Certification) and an *Oncology Pharmacist* (or *Hospital Pharmacist with Oncology Training*) from the facility where the order was initiated.

14. Telephone orders for a full cycle of cancer chemotherapy are not acceptable.
 - a. Telephone orders may be given to hold or to restart or to change the date of any cancer chemotherapy dose(s). These orders will be written as a telephone physician order on the health record, following the institutional policy.
 - b. Telephone orders to change the dose of any cancer chemotherapy drug from the dose written on a hospital Physician Order Form will not be accepted and must be written on a new PPO or PPO-O by an *Oncologist* or *Oncologist Delegate*.
 - c. All telephone orders will be signed by the ordering physician within 24 hours, or as per institutional policy.
15. Each order for cancer chemotherapy will be verified and countersigned by a pharmacist prior to dispensing the drugs, and by a nurse, prior to administration of the drugs.
 - a. Whenever possible, the pharmacy verification and countersignature will be performed by an *Oncology Pharmacist* or a *Hospital Pharmacist with Oncology Training*; when neither of these are available, verification will be performed by another staff pharmacist.
 - b. Nursing verification and countersignature will be performed by a *Registered Nurse with Chemotherapy Certification*.

PROCEDURES

1. If cancer chemotherapy is transferred to another facility for administration, the *Oncologist* or *Oncologist Delegate* at the Cancer Care Program will note on the *Pre-Printed Order* (PPO) or *Generic Pre-Printed Order* (PPO-G) the facility where the chemotherapy is intended to be administered, and the name of the local physician (*Community Specialist* or *Community Physician*) responsible for this treatment.
 - a. It is the responsibility of the referring *Oncologist* or *Oncologist Delegate* to identify the local physician who will be supervising the chemotherapy, and to ensure that the local physician accepts this responsibility.
 - b. A list of local *Community Specialists* and *Community Physicians* experienced in chemotherapy delivery will be maintained and available for or in the district. *Cancer Care Nova Scotia*, in collaboration with each district, may also keep a list of physicians with district privileges.
2. If cancer chemotherapy administration is transferred to another facility, the *Oncologist* or *Community Specialist* will ensure that the facility where the chemotherapy is to be administered is appropriate for the regimen to be given and that the local physician will accept responsibility for the transfer.
 - a. The chemotherapy protocol or portion of the protocol under consideration will be compared against the *Level of Care* for cancer chemotherapy assigned to the treating facility. No regimen or portion of a protocol will be given if the facility does not have the applicable resources to safely deliver the treatment, as defined by the *Levels of*

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Care Criteria for Cancer Systemic Therapy

- b. A list of local facilities and their assigned *Levels of Care* for cancer chemotherapy will be maintained and available from *Cancer Care Nova Scotia*, in collaboration with each district.
3. If the patient has been assessed within one week by the consulting physician, the local physician should be satisfied that there is no change in the patient's status since that assessment, which could change the decision to administer chemotherapy.
 - a. If the local physician is not satisfied, or if the consultant assessment is more than one week prior to chemotherapy administration date, the local physician will re-assess the patient prior to initiation of a cancer chemotherapy protocol.
4. Prior to the administration of chemotherapy a pre-treatment nursing assessment will be completed. This includes:
 - a. Height and weight
 - b. Vital signs
 - c. Performance status (ECOG)
 - d. Physical / toxicity assessment
 - e. Assessment of the emotional, psychosocial and financial impact of the diagnosis and treatment on the patient and family
 - f. Assessment of the patient's (or *parent/guardian's*) understanding and learning needs
 - g. Patient (or *parent/guardian's*) teaching
5. Patients will be reviewed at least once with each cycle of cancer chemotherapy, and more often if the cycle duration exceeds 6 weeks.
6. The *Oncologist* or *Community Specialist* most responsible for cancer chemotherapy treatment) will obtain an informed consent, as per institutional policy.
 - a. If any portion of the chemotherapy will be administered at a different site, the physician should obtain a "Consent to Transfer Chemotherapy Treatment", when explaining to the patient the process by which care and treatment will be shared with a local physician and local hospital.
 - b. All informed consent discussions should be fully documented in the health record at each institution.
 - c. If the patient is offered a new treatment protocol, a new informed consent must be obtained.
7. On each PPO or PPO-G, the following criteria should be completed by the *Oncologist* or *Community Specialist* :
 - a. Lab & toxicity measurements to be taken
 - b. Patient diagnosis and performance status
 - c. Antiemetics, hydration, other supportive care measures
 - d. All systemic therapy (chemotherapy) drugs and doses (with both relative [mg/m² or mg/Kg] and absolute [total mg] dosages for each)
 - e. Date(s) to be administered
 - f. Complete sections for height, weight and/or body surface area (BSA) as indicated
 - g. Any pertinent notes or communications, particularly if dosage is altered

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from calculated amount, or if a chemotherapy drug is deleted, or if administration instructions are changed. These notes will be written in the Modifications section of the PSO. The rationale should be included in the note.

- h. Signature of the prescriber, legible printed name.
- i. Date ordered
- j. Patient addressograph imprint (or hospital identifier label, as approved by the DHA)
- k. Additional information required on each *Pre-Printed Order for Oral Chemotherapy (PPO-O) Form* includes:
 - i) An exact quantity for dispensing, with no repeats allowed for any chemotherapy agent
 - ii) Pertinent information for auxiliary labeling by the pharmacist and/or supportive care suggestions for educational reinforcement
 - iii) Specific starting date for self-administration
8. The *Registered Nurse with Chemotherapy Certification or Oncology Pharmacist (or Hospital Pharmacist with Oncology Training)* in any treatment facility will not accept or action orders with chemotherapy drug(s) added or the route of administration changed from those on the PPO
9. Any cancer chemotherapy order not written on a preprinted PPO must be assessed by the *Oncology Pharmacist or Hospital Pharmacist with Oncology Training* for safety issues, including dosing, preparation and administration details, and any evidence on the use of the regimen in the disease being treated. The first dose will not be administered until the assessment is completed.
 - a. For the purpose of ensuring safety in order verification, regimens not ordinarily used (and not included in the *Systemic Therapy Manual for Cancer Treatment*) will be accompanied with supporting documentation (reference citation should be included on the order form or in the physician's Progress Note).
10. For any non-formulary drugs, proper administrative approval will be required before the first dose may be administered at the local facility.
 - a. The *Provincial Cancer Drug Formulary* (in the *Systemic Therapy Manual for Cancer Treatment*) will be used to determine non-formulary status for chemotherapy agents. The District Health Authority Formulary should also be considered for chemotherapy agents administered within the treatment facility.
 - b. Administrative approval from the *CCNS Systemic Therapy Program* may be obtained by the *Oncologist or Community Specialist* prior to transmission of the order to another facility in a different health care district.
11. When completed, a copy of the PPO-O should be filed on the patient's health record.
12. If an order has been written in one setting (e.g. inpatient unit), and the patient is transferred to another setting (e.g. ambulatory unit):
 - a. The order form will be transferred along with the patient to the new setting. (If the patient's status has changed during treatment, the order

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should be reassessed by the responsible physician)

- b. If the order cannot be transferred with the patient, the portion of the order to be given in the new setting will be written on a new PPO, and the portion given in the previous setting will cross-referenced (i.e. date given and location).
13. In certain circumstances, where there is a formal written agreement between the physician and the oncology pharmacist, the PPO may be written by the oncology pharmacist, provided that:
 - a. The order is completed on an approved PPO
 - b. The order follows an ongoing course of therapy, and the initial order was written by an *Oncologist* or *Community Specialist*.
 - c. The order is completely reviewed and countersigned by the *Oncologist* or *Community Specialist*, to the satisfaction of the oncology pharmacist, in lieu of order verification by the oncology pharmacist prior to drug dispensing and administration.
 14. Prior to dispensing any cancer chemotherapy dose(s), the *Oncology Pharmacist* or a *Hospital Pharmacist with Oncology Training* or other hospital pharmacist (if no oncology-trained pharmacist available) will verify the chemotherapy order, including, as appropriate:
 - a. Recalculate or verify all doses, to confirm accuracy of calculations
 - b. Recalculate or verify BSA (BSA calculator or BSA Nomogram) or AUC for initial dosing with each course of chemotherapy
 - i) Recalculate or verify BSA for cycles within chemotherapy course if weight changes by >10% from baseline
 - ii) Recalculate or verify AUC with each cycle of chemotherapy (i.e. each dose of Carboplatin)
 - c. Monitor pertinent lab results with each cycle of chemotherapy (e.g. CBC, Serum Creatinine, LFT's)
 - i) For each regimen, lab results to monitor are noted on the PPO (and in the regimen monograph in the *Systemic Therapy Manual for Cancer Patients*)
 - ii) If current lab tests are unavailable (i.e. tests done since the previous cycle), contact the prescriber or *Oncology Nurse* to ensure lab tests were ordered, or reason why lab tests not ordered
 - d. Review toxicity assessment from the toxicity assessment form, nursing assessment or equivalent
 - i) Review toxicity assessment from the toxicity assessment form, nursing assessment or equivalent
 - ii) If current toxicity assessment are unavailable, contact the oncology nurse to ensure toxicity assessment were obtained, or reason why patient was not assessed for toxicities
 - iii) If toxicities not assessed, the pharmacist will either assess the toxicities with the patient, or ensure this is done by one of the oncology nursing staff
 - e. Confirm the patient's current diagnosis, to ensure a correct PPO has been used.
 - i) Also examine for other pertinent disease-related criteria which

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may be relevant for regimen selection

- f. Confirm and verify drugs, doses and routes, as ordered on the PPO or the PPO-G.
 - i) If any chemotherapy drug has been changed, the PPO will be rewritten for the proper regimen (or a PPO-G may be used)
 - ii) If any chemotherapy drug has been added, the PPO will be rewritten for the proper regimen (or a PPO-G may be used)
 - iii) If any chemotherapy drug has been removed, confirm the reason for the regimen change
 - iv) If any chemotherapy dosage has been changed, confirm the reason from prescriber
 - v) If there are any dosage increases or frequency increases, the PPO will be rewritten for the proper regimen (or a PPO-G may be used)
 - vi) If any supportive care drug or measure has been changed, confirm the reason for change from the prescriber or *Oncology Nurse*.
 - vii) If the chemotherapy is concurrent with radiotherapy, or any other treatment modality, the sequencing and appointment timing will be confirmed and clearly identified (including any time needed for travel arrangements). Appointment scheduling is a shared responsibility of nursing and clerical staff.
- g. For any take-home prescriptions (supportive care drugs, component of chemotherapy), the pharmacist (in collaboration with the nurse and physician) will ensure that an appropriate prescription is available for the patient to have the take-home medications dispensed
 - i) Where available, a *Pre-Printed Order for Oral Chemotherapy (PPO-O) Form* will be used to order oral chemotherapy.
 - ii) The pharmacist may also contact the patient's community pharmacy to ensure that the take-home medications are available locally, and can be dispensed in time for the first dose at home.
- h. Track chemotherapy and supportive care orders on Pharmacy Monitoring Form, if available in local hospital.
- i. Confirm and/or complete authorization forms for all non-formulary drugs (as listed in *Provincial Cancer Drug Formulary*, included in the *Systemic Therapy Manual for Cancer Treatment*)
 - i) Restricted or non-formulary drugs are to be held until full authorization has been completed and received by the verifying pharmacist.
- j. When all details have been confirmed, the pharmacist will verify the chemotherapy order by signing the prescription form. A copy of the prescription form, signed by the pharmacist, will be sent with the drugs (or sent to the chemotherapy administration unit/location) and kept on the health record.
- k. The verified prescription may be sent to the chemotherapy admixture service for drug preparation.

15. If cancer chemotherapy is transferred to another facility for administration, the order form (PPO or the PPO-G) will be reviewed, verified, and signed by an *Oncology Pharmacist or Hospital Pharmacist with Oncology Training at*

the initiating facility. The order is verified to meet quality criteria (similar to those as if the dose were to administered at the consultant facility), that include:

- a. The BSA or AUC (if used to calculate the dose).
 - b. Initial diagnosis, or change in diagnosis (e.g. stage change with progressive cancer).
 - i) Also examine for other criteria for regimen selection
 - c. Confirm and verify drugs, doses and routes, as ordered on the PPO or the PPO-G.
 - d. Dose is appropriate for the patient and treatment plan.
 - e. Documentation of any changes from the PPO, or issues identified with the PPO-G, and any discrepancies discussed and resolved with the consultant oncologist. This documentation will be copied and transmitted with the order to the local site for administration.
 - f. In addition, if the chemotherapy is to be administered at another facility within the district the oncology pharmacist will also review:
 - i) Current lab results
 - ii) Authorization forms for all non-formulary drugs have been completed by the oncologist or oncologist delegate
16. When the order is reviewed by an *Oncology Pharmacist* or *Hospital Pharmacist with Oncology Training* assigned to the Cancer Care Program, the review may be completed as follows:
- a. If an *Oncology Pharmacist* or *Hospital Pharmacist with Oncology Training* is assigned to clinical duties in the ambulatory clinic area where the consultation order is written, he/she will review this order while present in the clinic.
 - b. If there is no *Oncology Pharmacist* or *Hospital Pharmacist with Oncology Training* in the ambulatory clinic area, the order and health record will be transported to the oncology pharmacy satellite for verification
 - c. If the *Oncology Pharmacist* or *Hospital Pharmacist with Oncology Training* is unable to verify the order within a reasonable time, he/she may negotiate with another pharmacist or the *Oncology Nurse* to verify the order.
 - d. Verification will be completed before the end of that working day; if the order is written after normal operating hours for oncology pharmacy, it will be verified at the beginning of the next working day
17. When the order is reviewed and verified by an *Oncology Nurse*:
- a. The *Oncology Nurse* will triage orders, to identify orders to be administered at another institution
 - b. The order will be verified according to the above criteria and signed by the *Oncology Nurse*, as appropriate within the workflow of the *Oncology Nurse*.
 - c. If the *Oncology Nurse* is unable to verify the order within a reasonable time, he/she may negotiate with another *Oncology Nurse* or the *Oncology Pharmacist* (or *Hospital Pharmacist with Oncology Training*) to verify the order.
 - d. Verification will be completed before the end of that working day, if the

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order is generated after business hours for the *Oncology Nurse*, it will be verified at the beginning of the next working day

18. When the order has been verified and signed, it may be transmitted to the local facility by fax. The receipt of the transmitted order will be confirmed by the sender (i.e. telephone confirmation with the receiver). It is anticipated that the orders will be planned for administration at the other facility on a subsequent day, unless alternate arrangements have been made and fully communicated in advance.
 - a. A copy of the order may be given to the patient for delivery to the local administration facility, if the order has been verified before the patient leaves the consultant site to help reduce the chance of translation/transcription error at the other institution
19. Prior to dispensing any cancer chemotherapy dose(s) in a District Health Authority facility other than the initiating site, the local *Hospital Pharmacist with Oncology Training* (or staff pharmacist if not available) will verify the chemotherapy order, including, as appropriate:
 - a. Confirm that the PPO or PPO-G is co-signed by the *Community Physician with Chemotherapy Prescribing Privileges* (or, if the PPO or PPO-G was transcribed, that it is the same as the one sent by the consultant *Oncologist* or *Oncologist Delegate* (for the first cycle or course), or the correct PPO for subsequent cycles of courses, as identified in the treatment plan.
 - b. Confirm that the initial PPO has been verified by the oncology pharmacist at the consultant facility
 - i) For cycles subsequent to the initial cycle, perform the verification procedures, as outlined above
 - c. For any take-home prescriptions (supportive care drugs, component of chemotherapy), the pharmacist (in collaboration with the nurse) will ensure that an appropriate prescription is available for the patient to have the take-home medications dispensed
 - i) Where available, a *Pre-Printed Order for Oral Chemotherapy* (PPO-O) Form will be used to order oral chemotherapy.
 - ii) The pharmacist may also contact the patient's community pharmacy to ensure that the take-home medications are available locally, and can be dispensed in time for the first dose at home.
 - d. Confirm and/or complete authorization forms for all non-formulary drugs
 - i) Restricted or non-formulary drugs are to be held until full authorization has been completed and received by the verifying pharmacist.
 - e. When all details have been confirmed, the pharmacist will verify the chemotherapy order by signing the original prescription form.
 - f. The verified prescription may be sent to the chemotherapy admixture service for drug preparation.
20. If the pharmacy verification is performed at a location within the facility separate from the chemotherapy administration unit, the verifying pharmacist may use a fax copy of the original PPO or PPO-G, transmitted from the unit. When verification is completed, the copy may be refaxed back to the unit, with the words "Verified by Pharmacy" clearly affixed or written on the form

and the signature of the verifying pharmacist.

- a. The retransmitted copy will be kept on file in the patient's health record, along with the original copy.
 - b. The pharmacy will keep the copy used for verification in the pharmacy department records.
21. Prior to the administration of cancer chemotherapy in any District Health Authority facility, the *Registered Nurse with Chemotherapy Certification*, who is administering the chemotherapy, will:
- a. Complete the pre-treatment nursing assessment, or review the assessment if completed by another *Oncology Nurse*.
 - b. Ensure that the consent has been signed.
 - c. Recalculate the BSA or AUC (if used to calculate the dose).
 - d. Review lab results.
 - e. Verify that the dose or dosage range is appropriate for the patient and treatment plan using an approved reference. Always recalculate the dose or dosage range (especially for orders on a PPO-G).
 - f. Identify potential side effects (immediate, short and long term).
 - g. Verify with another registered nurse (or the pharmacist or physician, if another registered nurse is not available) that the information on the label on the chemotherapy drug matches the information on the physician order or medication record (Checking patient's name, patient identification number, drug name and dose).
 - h. Check that the full name and patient identification number on the label on the chemotherapy drug matches the full name and patient identification number on the patient's identification armband/tags or equivalent personal identification on the patient.
22. Prior to the administration of chemotherapy to any pediatric oncology patient, a pretreatment physician assessment will be completed. The assessment may be done by the pediatric oncologist at the tertiary facility. This includes:
- a. Review of the child's current history
 - b. Documentation of any current concerns
 - c. General physical examination with emphasis on potential toxicity or complications
 - d. Review of the child's chemotherapy plan and readiness to receive the current prescribed cycle of treatment
23. Any discrepancies must be documented and concerns discussed and resolved with the ordering physician prior to administration. If there is any discrepancy, the pharmacist or nurse will discuss this with the prescriber (or, for orders transferred to another Capital Health facility, the consultant *Oncologist* or *Oncologist Delegate*, as appropriate), and confirm any changes required as a result of the discrepancy resolution.
- a. The prescribing physician will be responsible to provide direction on the appropriate action upon notification of a discrepancy or abnormal finding (e.g. lab results, information from patient).
 - b. If there is a change, a new order may be initiated, at the discretion of the pharmacist and the prescriber. The replacement order may be a telephone order, or rewritten by the prescriber.
 - c. If an order or PPO is rewritten, the original order may be discarded (if

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the entire order is rewritten) or the changed portion on the original order will be crossed out and marked as "VOID", with cross-reference to the replacement order

- d. The action will be communicated to the patient, and documented on the patient's health record by the health care provider.
24. The *Registered Nurse with Chemotherapy Certification*, who administered the medication, will document all chemotherapy medications given on a medication record, but not on the PPO form.
25. For any patient who will provide self-care at home, following the chemotherapy treatment, including take-home prescriptions (for supportive care drugs, component of chemotherapy or other drugs), the nurse will (in collaboration with the pharmacist):
- a. ensure that an appropriate prescription (where available, a PPO-O Form) and the means to have it filled are available for the patient to have the take-home medications dispensed
 - b. provide appropriate education for self care at home, including review of side effects management, prescriptions, and other care requirements
 - c. the nurse may also contact the patient's community pharmacy to ensure that the take-home medications are available locally, and can be dispensed in time for the first dose at home.

NOTE: These Draft Policies and Procedures were under deliberation for district approval by each of the district Pharmacy & Therapeutics or Drugs & Therapeutics Committees at time of print. Each district will formally approve these policies in due course, but there may be minor modifications in some districts to reflect their own process for related components (e.g. approval process for standing orders, obtaining consent, etc.) and their own policy cross-reference numbers where appropriate.

LEVELS OF CARE FOR SYSTEMIC THERAPY IN NOVA SCOTIA HOSPITALS

Systemic therapy for cancer includes many types of drugs used alone or in combination with other treatment modalities (e.g. surgery, radiotherapy). Chemotherapy drugs, a major component of cancer systemic therapy, are potentially hazardous to both patients and health care workers. Safety is of paramount importance in the use of systemic therapy for cancer treatment. For patients, most chemotherapy drugs are given at doses very close to toxic doses (i.e. narrow therapeutic window). Adverse reactions may be predictable or idiosyncratic, and must be appropriately managed when these occur. Tight controls must exist for the ordering and administration of these agents to avoid the potential for error. In addition, many drugs may cause serious adverse events during or shortly after administration.

Delivery of systemic therapy can and should occur in locations as close to home as possible including appropriate local community hospitals, regional hospitals, and provincial tertiary hospitals. The Systemic Therapy Levels of Care criteria have been developed to assist District Health Authorities (DHAs) and other providers of systemic therapy determine the types of services that can be safely provided in any given location. The fundamental principle behind these criteria is safety first. Guidelines on the safe administration of cancer chemotherapy, as published by the Institute for Safe Medication Practices (ISMP), have been applied to the development of these criteria. The levels of care criteria include ensuring that staff have developed and maintain the appropriate competencies. At this point in time, (spring 2005), some of the education programs referenced have not yet been developed. CCNS is committed to developing these programs and working with DHAs and others to provide the appropriate training to staff.

The plan for Systemic Therapy Levels of Care separates hospital delivery/administration sites into several levels, based on the acuity and/or complexity of the therapy to be given, the physical facilities at the delivery site, the number of staff and training of that staff to deliver the medications and provide patient supportive care, and the credentialing of the medical staff and other health professionals monitoring the treatment. In addition, the management of oncologic emergencies is included in the Levels of Care criteria. Regimens listed in the **Systemic Therapy Manual for Cancer Patients** are assigned levels as appropriate.

The primary guiding principle for assignment of any drug to a Level is optimal patient safety. No institution is obliged to deliver every medication or regimen within the assigned level, if this is not felt to be safe. No facility may deliver any medication or regimen rated at a higher level, without prior authorization from the DHA.

A Levels of Care standard for management of pediatric hematology/oncology patients has been developed by APPHON (the Atlantic Provinces Pediatric Hematology/Oncology Network). When systemic therapy is given to pediatric cancer patients, these criteria must also be considered in conjunction with the Systemic Therapy Levels of Care criteria.

Definitions for Systemic Therapy Levels of Care:

Community /Home Level (not a Hospital) - Systemic therapy which may be self-administered (e.g. oral medications), or given in a community setting (e.g. physician's office) but does not require hospital services

Basic Level Hospital - Basic chemotherapy and other systemic therapies, which do not require complicated adverse effect management. Treatments must be administered within a health care institution (i.e. hospital). Presence of additional resources and expertise may be considered for allowance of selected Intermediate level regimens, as negotiated with CCNS certification.

Intermediate Level Hospital - Chemotherapy regimens that include agents where more specialized nursing skills or volume of activity (to maintain competence) are needed. Agents at this level include:

- Vesicant agents (eg. anthracycline agents, vinca alkaloids)
- Agents which require active hydration support (e.g. platinum salts)
- Agents with a high risk of hypersensitivity reactions or administration-related reactions (e.g. monoclonal antibodies, biologic agents, taxanes irinotecan)

Although each of these categories require different safety measures in an Intermediate Level Hospital, it is felt that hospitals at this level will likely meet all of the criteria for this level (e.g. a hospital large enough to host an ICU will also likely perform enough chemotherapy treatments to maintain nursing competence, etc.). Specific hospitals will be identified through the implementation phase of this project. Presence of additional resources and expertise may be considered for allowance of selected Advanced level regimens, as negotiated with CCNS certification.

Advanced Level Hospital - Regimens that should be given under the direct supervision of a medical oncologist, hematologist, gynecologic oncologist or urologist (as determined by the appropriate Cancer Site Team); Regimens given concurrently with radiotherapy (Advanced level during portion of chemotherapy given concurrently with radiotherapy- other portions of treatment may be rated at a different level)

Specialized Level Hospital - Regimens that require specialized facility resources (e.g. BMT support, special laboratory support such as Methotrexate levels) or multidisciplinary specialist teams (e.g. acute leukemia service, stem cell transplant service, oral-maxillofacial cancer team, neuro-oncology team).

The Levels of Care criteria are divided into categories, which are defined below.

1. Health Professionals

The Levels of Care criteria describe health human resource expectations for each level. An emphasis is placed upon the training and competence of individual practitioners, with greater training expected for higher levels. Some basic skills and training are required for any chemotherapy ordering, preparation or administration. Education and training may already exist. Where the education does not currently exist, CCNS will develop and facilitate delivery of appropriate programs and personnel certification. This will include required participation in certain modules (to be confirmed) of the CCNS Oncology Education for Health Professional Interprofessional Core Curriculum (ICC) such as

Chemotherapy, Oncologic Emergencies and Symptom Management (2 modules).

It is harder to determine appropriate numbers of each health care professional proportionate to workload, especially when less than one person is required for any given category. The health human resource numbers are not included within the Levels of Care criteria. Any facility providing systemic therapy must have sufficient numbers of qualified staff to ensure sustainable service, for instance during vacation periods or absences due to illness.

2. Physical Facilities

The general expectations for physical facilities are described in the Levels of Care criteria. A sample estimate for space and furnishings for a Basic Level or Intermediate Level facility is described in the following pages, as adopted from planning documentation used by outreach oncology affiliation agreements from some Cancer Care Ontario cancer centres. This information will be helpful for local sites to identify areas of potential improvement.

3. Organizational Support

Systemic therapy is a high-risk enterprise within district health authorities, and it is often a shared responsibility between organizations. It is important for optimal patient safety that organizations operate according to provincial standards and are consistently with one another. While each district is accountable for the services provided within the district, provincial policies and programs are designed to enhance continuity of care. *Cancer Care Nova Scotia* is mandated to work with each district to assist with training, and standards development and compliance, as appropriate.

4. Supportive Care

Systemic therapy includes more than just the administration of cytotoxic chemotherapy. The drugs and regimens can cause toxic adverse reactions which must be managed appropriately. Some predictable types of drug toxicity may be prevented with prophylactic supportive measures. Cancer patients have many supportive care needs throughout the cancer continuum. While it is beyond the scope of the Systemic Therapy Levels of Care model to address the entirety of supportive care, those supportive care needs most common for systemic therapy patients are identified. These should be considered in the broader scope of all supportive care needs and issues. Supportive care is divided (for ease of assessment and service planning) into 4 major categories: informational needs; psychosocial/emotional needs; physical needs, and practical needs. While most of these needs are not specific to Levels of Care, some supportive care services may be Level-specific.

5. Management of Oncologic Emergencies

Oncologic emergencies is another domain that is not specific to systemic therapy. Processes to manage oncologic emergencies, however, are mandatory for any institution providing systemic therapy to cancer patients. There must be effective communications between specialists and general practitioners as needed for management of oncologic emergencies when these occur in the patients' home communities. These processes are described briefly.

6. Provincial Cancer Drug Formulary

Drugs used for the systemic therapy of cancer are listed in a single formulary for adoption by District Health Authorities. Additions, deletions and modifications to this formulary will be the responsibility of the Cancer Systemic Therapy Advisory Committee, of the Department of Health. Certain drugs may be listed with site-specific or indication-specific restrictions (or both), depending upon the decision of this committee. Site-specific restrictions relate to the Systemic Therapy Levels of Care Criteria, as identified above. Indication-specific restrictions generally apply to new agents and/or expensive agents, with an emphasis on evidence-based recommendations for use. The preliminary Provincial Cancer Drug Formulary is included in Appendix 5, listing Levels for individual drugs.

7. Regimen Monographs – Systemic Therapy Manual for Cancer Treatment

Drugs used alone or in combination are listed in the **CCNS Systemic Therapy Manual** as disease- or indication-specific regimens. Each regimen is assigned a level of care designation, usually relative to the drug with the most stringent single agent level. Some regimens are given higher listing due to the specialty nature of the cancer disease under treatment, or to the need for concurrent treatment (e.g. radiotherapy). These regimens should only be delivered in hospitals with a level of care rating the same or greater than that assigned to the regimen.

8. Systemic Therapy Levels of Care Criteria

See following pages.

LEVELS OF CARE CRITERIA

	Basic Level Hospital	Intermediate Level Hospital
Description	• Basic chemotherapy and other systemic therapies, that do not require complicated adverse effect management. • Treatment could be delivered on prescheduled "chemotherapy clinic" days	• Higher volume of visits, usually in Regional Hospital setting • Chemotherapy regimens, that include agents for which more specialized nursing skills or volume of activity (to maintain competence) are needed. • Provides Basic Level systemic therapy also
Physical Facility	• Space for chemo administration which allows for limited distractions during administration • IV equipment for simple ambulatory drug treatments • Easy access to spill kits, supplies for decontamination • Rapid access to supportive drugs for treatment of extravasation • Rapid access to equipment/ drugs for resuscitation and anaphylaxis • On-site pharmacy with biological safety cabinet and related equipment • Access to basic laboratory tests/results • When available, CCNS certified site	Basic Level, plus: • Dedicated chemo treatment area adequate for volume of treatment visits • IV equipment for ambulatory or inpatient infusional drug treatments (e.g. Infusors); able to access central venous catheters (e.g. Port-a-Caths, Hickman catheters) • Intensive care services available on-site • Hospital should have diagnostic imaging and pathology support • When available, CCNS certified site

APPENDIX 3A

Advanced Level Hospital	Specialized Level Hospital	Community/Home Level
• Very high volume of visits, including ambulatory cancer centre, inpatient oncology beds and radiotherapy services on site- tertiary hospital • Chemotherapy regimens, that include agents for which additional specialized nursing skills or volume of activity are needed, or that must be administered in dedicated oncology inpatient beds. • Most types of cancer are treated at this site • Provides Intermediate Level systemic therapy also	• Regimens which require specialized facility resources (e.g. Bone Marrow Transplant/Stem Cell Transplant support, special laboratory support such as Methotrexate levels) or designated specialist teams (e.g. acute leukemia, stem cell transplant, oral-maxillofacial services, neuro-oncology team), which may include co-ordinated multidisciplinary care • May be specific to individual regimens and package of services required for delivery (e.g. local availability of other specialists, lab services) • Specialized programs for provincial or maritime provinces, eg. acute leukemia, BMT	• Aspects of care which do not require hospital services • Self administration of systemic therapy, drugs acquired from retail pharmacy (may also be given in hospital) • Injectable cytotoxic chemotherapy should NOT be initiated in home settings (unless stipulated otherwise in the Systemic Treatment Manual or pediatric regimen) • Treatments at home or in physicians' offices
Intermediate Level, plus • Inpatient oncology ward or dedicated beds for cancer patients with oncology nurses and oncologists available • Radiation therapy services on site (for regimens that require concurrent radiotherapy plus chemotherapy) • Specialized Diagnostic Imaging and Pathology for cancer diagnosis and staging	Same as Advanced Level • Bone Marrow Transplantation and Acute Leukemia service • Parenteral chemotherapy drugs should NOT be administered in the community setting (i.e. treatment should not be initiated and managed completely outside the hospital setting)	

LEVELS OF CARE CRITERIA

	Basic Level Hospital	Intermediate Level Hospital
Organizational Support	ALL LEVELS - Guidance by District Cancer Committee - Institutions at each level will offer service up to the assigned Level (e.g. Intermediate Level facilities can provide Basic and Intermediate level services) - Training of personnel supported by DHA (provision of adequate time and resources to acquire requisite training and maintenance of competence as per CCNS guidelines) - DHA will ensure adequate physical facilities and certified staffing for the level when available, voluntary certification of level by CCNS Systemic Therapy Program - Compliance with provincial Policies and Procedures on Cancer Systemic Therapy (e.g. Ordering Cancer Chemotherapy Policies and Procedures) - DHA/CCNS will audit sites for compliance with criteria for assigned Level of Care - Co-ordination of district hospital formulary with provincial oncology formulary, synchronization of provincial systemic therapy policies and procedures with local policies and procedures - Adoption of provincial standing orders for cancer systemic therapy regimens, appropriate to treatment level(s)	
Medical Staff	- All cancer chemotherapy should be ordered only by or in consultation with an Oncologist - At least one Community Physician to supervise chemo admin. on site or very readily available during administration visits - Physicians will NOT prepare cytotoxic chemotherapy doses - When available, completion of training program; participation in ICC (CCNS Interprofessional Core Curriculum for cancer care) is encouraged	Human Resources - All cancer chemotherapy should be ordered only by or in consultation with an Oncologist - If chemo is ordered without consultation by an oncologist (not recommended), this must be done by a Community Specialist with appropriate privileges in the district - At least one Community Physician or Community Specialist to supervise chemo admin on site during administration visits (may be responsible for chemo treatment unit) - May have Medical Oncology outreach support - Participation in continuing education and multidisciplinary rounds as available

APPENDIX 3A

Advanced Level Hospital	Specialized Level Hospital	Community/Home Level
• Provide expertise to provincial Cancer Site Teams for developing standard systemic therapy regimens and protocols • Receive provincial referrals for advanced level care patients, facilitate referrals to local communities for basic level and intermediate level care patients • Assist in training of health care professionals across province		• Maintenance of open communications with organized health care facilities and involved health care professionals
• <i>Medical Oncologists</i> and <i>Radiation Oncologists</i> on staff & available around the clock; may have <i>Hematologists</i> and/or <i>Surgical Oncologists</i> on staff & available around the clock • Regular participation in multidisciplinary rounds and continuing education for oncology	Same as Advanced Level • Oncologists have developed specific sub-specialized practices	• Family physicians- supportive care in collaboration with oncology specialist • Community specialists (e.g. surgeons, internists)- Office procedures for cancer patients within scope of service • Participation in ICC is encouraged

LEVELS OF CARE CRITERIA

	Basic Level Hospital	Intermediate Level Hospital
Registered Nurses	• At least two <i>Nurses with Chemotherapy Certification</i> • During administration of chemotherapy, the nurse will not be assigned to other responsibilities • If only one <i>Nurse with Chemotherapy Certification</i> is available, chemo to be checked by another nurse, physician or pharmacist- consultation support must be readily available • Nurses will NOT prepare injectable cytotoxic chemotherapy doses • Participation in ICC is encouraged	Human Resources • At least two dedicated <i>Nurses with Chemotherapy Certification</i> working in chemo unit at all patient care • Nurses will NOT prepare injectable cytotoxic chemotherapy doses • During administration of chemotherapy, the nurse will not be assigned to other responsibilities • Adequate number of patient treatment visits to maintain competence in managing vesicant administration, hypersensitivity reactions • Continuing education participation • Participation in ICC is required
Pharmacy	• On-site pharmacist (& technician?) with <i>Basic Oncology Pharmacy Training</i> (oncology order verification and chemo preparation) • Technician trained in chemo preparation, if available • All chemotherapy will be prepared by a pharmacy service, with at least one pharmacist and one technician (or a second pharmacist) involved • Access to pharmacist by phone & fax for consultation and order verification • All chemo orders verified by pharmacist within district • Participation in ICC is encouraged	• At least one <i>Hospital Pharmacist with Oncology Training</i> • At least one other pharmacist with <i>Basic Oncology Pharmacy Training</i> (for back-up) and at least two technicians trained in chemo preparation • Participation in continuing education program

APPENDIX 3A

Advanced Level Hospital	Specialized Level Hospital	Community/Home Level
• Adequate numbers of Nurses with Chemotherapy Certification to support all chemo order verification and drug administration needs • Adequate numbers of Oncology Nurse(s) and Clinical Nurse Specialists/Nurse Educators to provide full nursing service for inpatients & outpatients • Support to nurses and other health professionals providing Basic and Intermediate Levels of Systemic Therapy (as needed) • Participation in continuing education for oncology	Same as Advanced Level • Clinical Nurse Specialists/Nurse Educators to support nursing staff in sub-specialized areas	• Community or home care nursing (including LTC) in collaboration with oncology specialists • Supportive care measures during active treatment phase • Basic knowledge of cancer care • Participation in ICC is encouraged
Same as Intermediate Level, plus; • Adequate numbers of pharmacists and technicians to support all chemo order verification & drug preparation needs • At least one Oncology Pharmacy Specialist and adequate Hospital Pharmacists with Oncology Training to provide full clinical service for inpatients & outpatients • Support to pharmacists and other health professionals providing Basic and Intermediate Levels of Systemic Therapy (as needed)	Same as Advanced Level plus; • At least one Oncology Pharmacy Specialist to provide full clinical service for appropriate sub-specialty areas	• Retail pharmacists-dispensing systemic and supportive care drugs, as directed in standing orders or other prescription, verification of oral chemotherapy orders, patient counselling on medications • Basic knowledge of cancer care • Participation in ICC is encouraged

LEVELS OF CARE CRITERIA

	All Levels
Other Human Resources (including Supportive Care)	• Adequate clerical support personnel for patient scheduling • Adequate health records personnel support to supply health records in a timely fashion for ambulatory patient care (and inpatient care when necessary) • All patients receiving systemic therapy should have access to supportive care professionals and services based on their needs—either locally, within the district, or, if appropriate from the tertiary site
	• There is a Cancer Patient Navigator in each district. Cancer patients should be referred to the local Cancer Patient Navigator for supportive care needs, as appropriate* Psychosocial and other supportive care services offered to patients according to guidelines by the Supportive Care CST • Access to psychosocial support services within the district, which may include social work, psychology/psychiatry, psychosocial counselors, dietitians, occupational therapy, physiotherapy, and others • Health care professionals (including pastoral care) and volunteers trained in Palliative Care may assist with supportive care needs • Referral to advanced level services as necessary for psychosocial and rehabilitative care • Peer and family support groups for lay psychosocial support • Home caregiver support, may include homemaker or home care services
Supportive Care Services	<u>Information Needs</u> • Initiation of patient education if new treatment, or reinforcement if education provided elsewhere
	• Use of all approved cancer patient information material, including Living Well with Cancer and Medication Info Sheets, as appropriate • Access to experts for referral of difficult questions (e.g. Medical Oncologists, Hematologists, Oncology Nurses, Oncology Pharmacy Specialists) • Development of patient educational materials, as needed
	<u>Psychological/Emotional Needs</u> • General psychological and emotional support integrated into routine patient care; involvement of other supportive care professionals (see above) as appropriate and available
	<u>Practical Needs</u> • Social work involvement to assist in resolution of practical/financial difficulties; dietitian referral for nutritional problems; occupational therapy/physiotherapy for specific rehabilitation problems; access to palliative care team, pharmacist assistance with medication acquisition, insurance coverage, medication counseling • Coordination of integrated care plan by primary oncology team, to access services close to home or at tertiary centre, as appropriate
	<u>Physical Needs</u> • General medical care for common symptom management • Communication with and involvement of family physician for regular management of medical care/follow up in collaboration with oncology specialists

APPENDIX 3A

Advanced Level Hospital	Specialized Level Hospital	Community/Home Level
Same as All Levels, plus: • Multidisciplinary Psychosocial Oncology Team, including members with advanced training, available on referral or patient self-referral for unique cancer patient needs	Same as Advanced Level, plus: • Multidisciplinary team for comprehensive psychosocial support services unique to specialty populations (e.g. pediatrics, ASCT/ BMT patients, head & neck cancer patients, brain tumour patients and families, etc.)	
Same as All Levels, plus: • Psychosocial Oncology Team for referrals of complicated psychologic or emotional support	Same as Advanced Level	• Reinforcement of patient education initiated in hospital/clinic setting

LEVELS OF CARE CRITERIA

	Basic Level Hospital	Intermediate Level Hospital
Oncologic Emergencies	• Oncologic emergencies, including those associated with systemic therapy, will usually occur when patient is at home; basic management of emergencies must be available in all Levels of facility • Emergency department staff trained as appropriate for oncologic emergencies- encouraged to participate in relevant ICC module(s) • CCNS Symptom management guidelines (as available) will be followed • If patient has febrile neutropenia, empiric antibiotics at nearest Emergency Department according to guidelines, will require admission (unless otherwise instructed by oncologist) • Emergency surgery and intensive care services, as appropriate for district	

NOTE: These draft Levels of Care Criteria were under deliberation for approval by Cancer Care Nova Scotia and the health care districts at time of print. The criteria will be approved in due course, but there may be minor modifications in the final criteria after impact assessment has been completed. Drug and regimen assignment for Level of Care in the Provincial Cancer Drug Formulary will become the responsibility of the Cancer Systemic Therapy Advisory Committee, of the Department of Health.

APPENDIX 3A

Advanced Level Hospital	Specialized Level Hospital	Community/Home Level
		• Basic knowledge of oncologic emergencies and appropriate treatment • Rapid access to oncology specialists and/or Cancer Centre as needed for urgent specialist care • Participation in ICC is encouraged

9. Summary:

The Systemic Therapy Levels of Care criteria provide a model and a provincial standard for delivery of this hazardous treatment to cancer patients. With these criteria, District Health Authorities can plan their service delivery and monitor the quality of care through adherence to provincial standards. Other components also contribute to quality and safety of systemic therapy delivery, including:

- o the provincial policies and procedures (developed provincially and adopted by each district)
- o the provincial standard Physician Standing Orders for cancer systemic therapy
- o the **Systemic Therapy Manual for Cancer Patients** (as a consistent information source)
- o the Medication Info Sheets and other provincial patient education resources

Staff qualifications are supported by education and certification programs available or under development in partnership with *Cancer Care Nova Scotia*.

A key principle in this package of programs and initiatives is consistent standards across the province, with accountabilities at the DHA level. *Cancer Care Nova Scotia* is mandated and committed to assist each district, as standards are developed and implemented. It is expected that the full set of criteria will be implemented over time as resources and supporting programs or services become available within the province. Each district is expected to achieve the standards as soon as reasonably achievable.

PROVINCIAL CANCER DRUG FORMULARY**Introduction:**

The Provincial Cancer Drug Formulary is a listing of drugs used for treatment of cancer, and their status in hospitals at each level of care. This provincial formulary is suggested as the appropriate listing of cancer treatment drugs, to synchronize with the Levels of Care criteria, the Systemic Therapy Manual listing of specific regimens, and provincial policies and procedures. Health care districts may have individual hospitals in any of the levels of care categories. Drugs listed in the formulary may be restricted to certain levels, due to the risks during administration and/or the need for various resources during administration (including highly specialized teams for certain medications or treatment regimens). Certain drugs are restricted to specific indications, as indicated in practice guidelines. Other drugs may be excluded from the formulary, or may not yet be available on the Canadian market (but possibly available through a special access program). These are indicated in the formulary.

Individual health care districts may list drugs on their formularies as they determine appropriate.

Agents used for treatment or support of pediatric cancer patients may be available on a case-by-case basis, under specific instruction by Pediatric Oncology Service, IWK Health Centre

FORMULARY STATUS CODES:**Level Restriction:**

- Drug restricted to administration only at institution at designated level or higher, due to safety issues in regional and/or community hospitals.

Indication Restriction:

- Drug with specific indications and/or guideline criteria for use, listed as restricted in **Provincial Cancer Drug Formulary**. Level restrictions may still apply.

Non-Formulary:

- Not listed as a formulary benefit. Level restrictions may still apply.

Not Available:

- Drug not approved by Health Canada; may be available through Special Access Program. Level restrictions may still apply.

Provincial Cancer Drug Formulary

Agent	Level-Specific Formulary Status			
	Basic	Intermediate	Advanced	Specialized
Injectable Antineoplastic Agents				
Alemtuzumab <i>CamPath</i>	A Not Available- Level Restriction	Not Available- Level Restriction	Not Available	Not Available
Asparaginase (L-asparaginase) <i>Kidrolase</i>	I Level Restriction	Available	Available	Available
Bacillus Calmette- Guérin (BCG) <i>OncoTICE</i>	B Available (In closed system for bladder instillation)	Available	Available	Available
Bleomycin <i>Blenoxane</i>	B Available	Available	Available	Available
Carboplatin <i>Paraplatin-A</i>	I Level Restriction	Available	Available	Available
Carmustine <i>BiCNU</i>	I Level Restriction	Available	Available	Available
Cisplatin <i>Platinol-AQ</i>	I Level Restriction	Available	Available	Available
Cladribine <i>Leustatin</i>	I Level Restriction	Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction
Cyclophosphamide <i>Cytoxan, Procytox</i>	B Available	Available	Available	Available
Cytarabine low dose <i>Cytosar</i>	B Available	Available	Available	Available
Cytarabine High Dose	A Level Restriction ($\geq 500 \text{ mg/m}^2$)	Level Restriction ($\geq 500 \text{ mg/m}^2$)	Available	Available
Cytarabine Intrathecal	A Level Restriction	Level Restriction	Available	Available
Dacarbazine <i>DTIC</i>	I Level Restriction	Available	Available	Available
Dactinomycin <i>Cosmegen</i>	I Level Restriction	Available	Available	Available
Daunorubicin <i>Cerubidine</i>	I Level Restriction	Available	Available	Available
Docetaxel <i>Taxotere</i>	I Level Restriction	Indication Restriction	Indication Restriction	Indication Restriction
Doxorubicin <i>Adriamycin PFS</i>	I Level Restriction	Available	Available	Available
Epirubicin <i>Pharmorubicin</i>	I Level Restriction	Available	Available	Available
Etoposide (VP-16) <i>Vepesid</i>	I Level Restriction	Available	Available	Available
Fludarabine <i>Fludara</i>	B Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction

Provincial Cancer Drug Formulary

Agent	Level-Specific Formulary Status			
	Basic	Intermediate	Advanced	Specialized
Injectable Antineoplastic Agents				
Fluorouracil (5-fluorouracil, 5-FU) <i>Adrucil</i>	B Available	Available	Available	Available
Gemcitabine <i>Gemzar</i>	B Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction
Gemtuzumab <i>Mylotarg</i>	A Not Available- Level Restriction	Not Available- Level Restriction	Not Available	Not Available
Idarubicin <i>Idamycin</i>	I Level Restriction	Available	Available	Available
Ifosfamide <i>Ifex</i>	A Level Restriction	Level Restriction	Available	Available
Interferon alfa-2b High Dose IV <i>Intron A</i>	I Level Restriction	Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction
Interferon alfa-2b Low Dose IV/SC	B Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction
Interferon alfa-2b Intravesical	B Non-Formulary Indication Restriction	Non-Formulary Indication Restriction	Non-Formulary Indication Restriction	Non-Formulary Indication Restriction
Irinotecan <i>Camptosar</i>	I Level Restriction	Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction
Leucovorin	B Available	Available	Available	Available
Liposomal Cytarabine <i>Depocyt</i>	A Level Restriction	Level Restriction	Non-Formulary	Non-Formulary
Liposomal Daunorubicin <i>DaunoXome</i>	A Not Available- Level Restriction	Not Available- Level Restriction	Not Available	Not Available
Liposomal Doxorubicin (Pegylated) <i>Caelyx</i>	I Level Restriction	Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction
Mechlorethamine (nitrogen mustard) <i>Mustargen</i>	I Level Restriction	Available	Available	Available
Melphalan <i>Alkeran</i>	A Level Restriction	Level Restriction	Available	Available
Methotrexate Low Dose <i>Methotrexate</i>	B Available Level Restriction ($\geq 100 \text{ mg/m}^2$)	Available Level Restriction ($\geq 100 \text{ mg/m}^2$)	Available Level Restriction ($\geq 100 \text{ mg/m}^2$)	Available Available

Provincial Cancer Drug Formulary

Agent	Level-Specific Formulary Status			
	Basic	Intermediate	Advanced	Specialized
<u>Injectable Antineoplastic Agents</u>				
Methotrexate	S Level	Level	Level	Available
High Dose	Restriction	Restriction	Restriction	
Methotrexate	A Level	Level	Available	Available
Intrathecal	Restriction	Restriction		
Mitomycin	I Level	Available	Available	Available
<i>Mutamycin</i>	Restriction			
Mitoxantrone	I Level	Available	Available	Available
<i>Novantrone</i>	Restriction			
Oxaliplatin	I Not Available- Level	Not Available	Not Available	Not Available
<i>Eloxatin</i>	Restriction			
Paclitaxel	I Level	Available-	Available-	Available-
<i>Taxol</i>	Restriction	Indication Restriction	Indication Restriction	Indication Restriction
Pemetrexed	I Level	Available-	Available-	Available-
<i>Alimta</i>	Restriction	Indication Restriction	Indication Restriction	Indication Restriction
Raltitrexed	B Indication	Indication	Indication	Indication
<i>Tomudex</i>	Restriction	Restriction	Restriction	Restriction
Rituximab	I Level	Available-	Available-	Available-
<i>Rituxan</i>	Restriction	Indication Restriction	Indication Restriction	Indication Restriction
Streptozocin	I Level	Available	Available	Available
<i>Zanosar</i>	Restriction			
Thiotepa	I Level	Available	Available	Available
	Restriction			
Topotecan	I Level	Available-	Available-	Available-
<i>Hycamtin</i>	Restriction	Indication Restriction	Indication Restriction	Indication Restriction
Trastuzumab	B If no reaction	First doses at	Available-	Available-
<i>Herceptin</i>	first dose(s) Indication Restriction	Intermediate Indication Restriction	Indication Restriction	Indication Restriction
Valrubicin	I Non-Formulary	Non-Formulary	Non-Formulary	Non-Formulary
<i>Valtatin</i>	Level Restriction			
Vinblastine	I Level	Available	Available	Available
<i>Velbe</i>	Restriction			
Vincristine	I Level	Available	Available	Available
<i>Oncovin</i>	Restriction			
Vinorelbine	I Level	Available-	Available-	Available-
<i>Navelbine</i>	Restriction	Indication Restriction	Indication Restriction	Indication Restriction

Provincial Cancer Drug Formulary

Agent	Level-Specific Formulary Status			
	Basic	Intermediate	Advanced	Specialized
For in-patient nts during				
Busulfan Low Dose <i>Myleran</i>	B Available	Available	Available	Available
Busulfan High Dose <i>Myleran</i>	S Level Restriction	Level Restriction	Level Restriction	Available
Capecitabine <i>Xeloda</i>	B Available-Indication Restriction	Available-Indication Restriction	Available-Indication Restriction	Available-Indication Restriction
Chlorambucil <i>Leukeran</i>	B Available	Available	Available	Available
Cyclophosphamide <i>Cytoxan, Procytox</i>	B Available	Available	Available	Available
Etoposide (VP-16) <i>Vepesid</i>	B Available	Available	Available	Available
Hydroxyurea <i>Hidrea</i>	B Available	Available	Available	Available
Imatinib Mesylate <i>Gleevec</i>	B Available-Indication Restriction	Available-Indication Restriction	Available-Indication Restriction	Available-Indication Restriction
Leucovorin	B Available	Available	Available	Available
Lomustine (CCNU) <i>CeeNU</i>	B Available	Available	Available	Available
Melphalan <i>Alkeran</i>	B Available	Available	Available	Available
Mercaptopurine <i>Purinethol</i>	B Available	Available	Available	Available
Methotrexate <i>Rheumatrex, Methotrexate</i>	B Available	Available	Available	Available
Mitotane <i>Lysodren</i>	B Non-Formulary	Non-Formulary	Non-Formulary	Non-Formulary
Procarbazine <i>Natulan</i>	B Available	Available	Available	Available
Temozolomide <i>Temodal</i>	B Available-Indication Restriction	Available-Indication Restriction	Available-Indication Restriction	Available-Indication Restriction
Thioguanine <i>Lanvis</i>	B Available	Available	Available	Available
Tretinoin (all-trans retinoic acid) <i>Vesanoid</i>	S Level Restriction	Level Restriction	Level Restriction	Available

Provincial Cancer Drug Formulary

Agent	Level-Specific Formulary Status			
	Basic	Intermediate	Advanced	Specialized
Supportive Care Agents				
<i>For in-patient use or administration to ambulatory patients during treatment visit only</i>				
Ancestim <i>Stemgen</i>	S Level Restriction	Level Restriction	Level Restriction	Available- Indication Restriction
Aprepitant <i>Emend</i>	B Not Available	Not Available	Not Available	Not Available
Clodronate	B Available	Available	Available	Available
Dexamethasone	B Available	Available	Available	Available
Dexrazoxane <i>Zinecard</i>	I Level Restriction	Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction
Dolasetron <i>Anzemet</i>	B Non-Formulary	Non-Formulary	Non-Formulary	Non-Formulary
Domperidone <i>Motilium</i>	B Available	Available	Available	Available
Dronabinol <i>Marinol</i>	B Non-Formulary	Non-Formulary	Non-Formulary	Non-Formulary
Epoetin <i>Eprex</i>	B Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction
Filgrastim <i>Neupogen</i>	B Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction
Granisetron <i>Kytril</i>	B Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction
Loperamide <i>Imodium</i>	B Available	Available	Available	Available
Mannitol	B Available	Available	Available	Available
Mesna <i>Uromitexan</i>	B Available	Available	Available	Available
Methylprednisolone <i>Medrol</i>	B Available	Available	Available	Available
Metoclopramide <i>Maxeran</i>	B Available	Available	Available	Available
Nabilone <i>Cesamet</i>	B Available	Available	Available	Available
Octreotide <i>Sandostatin</i>	B Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction
Ondansetron <i>Zofran</i>	B Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction
Pamidronate <i>Aredia</i>	B Indication Restriction	Indication Restriction	Indication Restriction	Indication Restriction

Provincial Cancer Drug Formulary

Agent	Level-Specific Formulary Status			
	Basic	Intermediate	Advanced	Specialized
Supportive Care Agents				
<i>For in-patient use or administration to ambulatory patients during treatment visit only</i>				
Pegfilgrastim <i>Neulasta</i>	B Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction
Pilocarpine <i>Salagen</i>	B Available	Available	Available	Available
Prochlorperazine <i>Stemetil</i>	B Available	Available	Available	Available
Rasburicase <i>Vasurtec</i>	A Non-Formulary Level Restriction	Non-Formulary Level Restriction	Non-Formulary	Non-Formulary
Thalidomide <i>Thalomid</i>	B Not Available	Not Available	Not Available	Not Available
Zoledronic Acid <i>Zometa</i>	B Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction	Available- Indication Restriction
Hormone Agents				
<i>For in-patient use or administration to ambulatory patients during treatment visit only</i>				
Anastrozole <i>Arimidex</i>	B Available	Available	Available	Available
Bicalutamide <i>Casodex</i>	B Available	Available	Available	Available
Buserelin <i>Suprefact</i>	B Available	Available	Available	Available
Cyproterone <i>Androcur</i>	B Available	Available	Available	Available
Estramustine <i>Emcyf</i>	B Available	Available	Available	Available
Exemestane <i>Aromasin</i>	B Available	Available	Available	Available
Flutamide <i>Euflex</i>	B Available	Available	Available	Available
Goserelin <i>Zoladex</i>	B Available	Available	Available	Available
Letrozole <i>Femara</i>	B Available	Available	Available	Available
Leuprolide acetate <i>Lupron</i>	B Available	Available	Available	Available
Megestrol <i>Megace</i>	B Available	Available	Available	Available
Nilutamide <i>Anandron</i>	B Available	Available	Available	Available
Tamoxifen <i>Nolvadex</i>	B Available	Available	Available	Available

Provincial Cancer Drug Formulary

Indication-Specific Restrictions

Drug	Indication Restrictions	Comments
Ancestim <i>Stemgen</i>	For mobilization of peripheral blood stem cells (PBSC) in high-dose chemotherapy [According to approved guidelines]	Level restriction- limited to hospital with stem cell transplantation program
Capecitabine <i>Xeloda</i>	- Treatment of metastatic breast cancer (MBC) patients after failure of standard therapy [According to approved guidelines] - Treatment of metastatic colorectal cancer (CRC) patients after failure of standard therapy	Initial order by oncologist or community specialist All orders on approved PSO [According to approved guidelines and/or approved physician standing orders]
Cladribine <i>Leustatin</i>	Treatment of Hairy Cell Leukemia (HCL): first-line, Waldenstrom's macroglobulinemia (WM): first-line therapy [According to approved guidelines]	Ordered by hematology specialist familiar with treatment of leukemias, only for patients meeting approved guidelines and/or approved physician standing orders
Dexrazoxane <i>Zinecard</i>	Cardiac protection with doxorubicin in metastatic breast cancer patients [According to approved guidelines]	Ordered by oncologist or community specialist For other cancers [Non HPB-approved indications], Non-Formulary Request Form must be completed
Docetaxel <i>Taxotere</i>	- Treatment of metastatic breast cancer (MBC) patients - As a single agent for second-line therapy of advanced non-small cell lung cancer (NSCLC) patients - As a single agent for treatment of hormone-refractory prostate cancer (HRPC) patients [According to approved guidelines]	Initial order by oncologist or community specialist For other indications [Non HPB-approved indications], Non-Formulary Request Form must be completed
Filgrastim (gCSF) <i>Neupogen</i>	<u>Primary use:</u> - for use in patients receiving chemotherapy with documented febrile neutropenia rate >50% <u>Secondary use:</u> - for prevention of febrile neutropenia in patients who have experienced febrile neutropenia, neutropenic sepsis or profound neutropenia, - to prevent dose reduction or dose delay (if previously occurred) - chronic neutropenia	Patients meeting the criteria for filgrastim use set forth by the Oncology Therapy Subcommittee (Capital Health) [Filgrastim Request Form must be completed in all instances]

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Indication-Specific Restrictions

Drug	Indication Restrictions	Comments
Filgrastim (continued)	• drug-induced neutropenia • neutropenia while awaiting bone marrow transplant • delayed engraftment • PBSC collection • autologous transplant [According to approved guidelines]	
Fludarabine <i>Fludara</i>	For use in patients with selected hematologic malignancies • Chronic Lymphocytic Leukemia (CLL) first-line therapy • Low grade Non-Hodgkins Lymphoma (NHL) second- or third-line therapy • Polymphocytic leukemia first-line therapy • Waldanstrom's macroglobulinemia (WM) first-line therapy • Fludarabine in combination with cyclophosphamide as the standard conditioning regimen for non-myeloablative allogenic transplantation [According to approved guidelines]	Ordered by specialist familiar with treatment of leukemias and lymphomas Patients meeting approved guidelinesand/or approved physician standing orders
Gemcitabine <i>Gemzar</i>	• Treatment of patients with unresectable or metastatic adenocarcinoma of the pancreas • Gemcitabine in combination with cisplatin is approved for the treatment of advanced or meta-static bladder cancer • Gemcitabine in combination with cisplatin in the treatment of advanced non-small cell lung cancer patients (NSCLC) patients [According to approved guidelines]	Initial order by oncologist or community specialist All orders on approved PSO [According to approved guidelinesand/or approved physician standing orders]
Granisetron <i>Kytril</i>	• Oncology patients receiving emetogenic therapy • With a history of intolerance or contraindication to conventional antiemetic agents	[According to approved CCNS guidelinesand/or approved physician standing orders] • Other non-cancer indications

Provincial Cancer Drug Formulary

Indication-Specific Restrictions

Drug	Indication Restrictions	Comments
Imatinib <i>Gleevec</i>	As a single agent in patients who have documented evidence of Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML), with an ECOG performance status of 0-2, who are: • In blast crisis OR • In accelerated phase OR • In chronic phase as first line treatment or after failure of interferon-alpha (IFN-α) therapy defined as: • a lack of hematologic response after 3 months of therapy • no cytogenetic response after 1 year of therapy • a documented severe intolerance to IFN-α • a hematologic relapse or cytogenetic progression after previous response to IFN-α therapy [According to approved guidelines] • Treatment of unresectable metastatic or advanced gastrointestinal stromal tumors (GIST) [According to approved guidelines]	Ordered by oncologist or hematology specialist familiar with treatment of leukemias or GIST [According to approved guidelines]
Interferon alfa-2b <i>Intron A</i>	• Adjuvant therapy in high-risk malignant melanoma patients • As a single agent for the treatment of metastatic renal cell carcinoma (RCC) in selected patients [According to approved guidelines]	Ordered by oncologist or hematology specialist familiar with treatment of leukemias
Irinotecan <i>Camptosar</i>	Treatment of metastatic colorectal cancer (MCRC) patients [According to approved guidelines]	Initial order by oncologist or community specialist in consultation with oncologist All orders on approved PSO [According to approved guidelines and/or approved physician standing orders]
Octreotide <i>Sandostatin</i>	• Severe chemotherapy-induced diarrhea uncontrolled by traditional agents • Management of malignant intestinal obstruction	[According to approved guidelines and/or approved physician standing orders]

Provincial Cancer Drug Formulary

Indication-Specific Restrictions

Drug	Indication Restrictions	Comments
Octreotide (continued)	• Control of symptoms in patients with carcinoid tumor, VIPomas, acromegaly • <i>Other non-cancer indications</i>	
Ondansetron Zofran	Patients, • Oncology patients receiving emetogenic therapy • <i>Scheduled to receive liver, abdominal or total body radiotherapy</i> • With a history of intolerance or contraindication to conventional antiemetic agents • <i>Other non-cancer indications</i>	[According to approved CCNS guidelinesand/or approved physician standing orders]
Paclitaxel Taxol	• Treatment of patients with advanced ovarian carcinoma including sub-optimal debulked (Stage IIB, IIC, III + IV), fallopian tube carcinoma and adjuvant high risk early disease. • Treatment of patients with metastatic carcinoma of unknown primary • In combination with carboplatin for advanced non-small cell lung cancer (NSCLC) or adjuvant treatment of Stage IIB NSCLC • Treatment of patients with recurrent or advanced endometrial carcinoma, high risk newly diagnosed (Stage IIIB or higher) or recurrent (combination therapy) • Treatment of patients with metastatic breast cancer in combination with trastuzumab • In combination with carboplatin in newly diagnosed high risk of relapse (Stage IIIB or higher) or recurrent endometrial cancer patients [According to approved guidelines]	Initial order by oncologist or community specialist in consultation with oncologist All orders on approved PSO [According to approved guidelinesand/or approved physician standing orders]
Raltitrexed Tomudex	Treatment of metastatic/advanced colorectal cancer (MCRC) patients [According to approved guidelines]	Initial order by oncologist or community specialist All orders on approved PSO Patients meeting approved guidelines

Provincial Cancer Drug Formulary

Indication-Specific Restrictions

Drug	Indication Restrictions	Comments
Rituximab <i>Rituxan</i>	Hematology Non-Hodgkin's Lymphoma [According to approved guidelinesand/or approved physician standing orders]	Ordered by hematology specialist familiar with treatment of lymphomas [According to approved guidelinesand/or approved physician standing orders]
Temozolomide <i>Temodal</i>	Treatment of patients with recurrent malignant gliomas [According to approved guidelines]	Ordered in consultation with neuro-oncologist Patients meeting approved guidelinesand/or approved physician standing orders
Thalidomide <i>Synovir</i>	Treatment of graft-versus-host disease [Special Access Program, Health Canada]	Level restriction- limited to hospital with stem cell transplantation program
Topotecan <i>Hycamtin</i>	Treatment of patients with recurrent ovarian cancer Second-line treatment of patients with small cell lung cancer (SCLC) [According to approved guidelines]	Initial order by oncologist or community specialist in consultation with oncologist All orders on approved PSO [According to approved guidelinesand/or approved physician standing orders]
Trastuzumab <i>Herceptin</i>	• Treatment of metastatic breast cancer patients [According to approved guidelines]	Initial order by oncologist or community specialist in consultation with oncologist All orders on approved PSO [According to approved guidelinesand/or approved physician standing orders]
Tretinoin (all-trans-retinoic acid) <i>Vesanoid</i>	Treatment of Acute Promyelocytic Leukemia (APL) patients [According to approved guidelines]	Ordered by hematology specialist familiar with treatment of leukemias Patients meeting approved guidelines and/or approved physician standing orders
Vinorelbine <i>Navelbine</i>	• Treatment of Non-small cell lung cancer (NSCLC) patients • Treatment of metastatic breast cancer (MBC) patients [According to approved guidelines]	Initial order by oncologist or community specialist in consultation with oncologist All orders on approved PSO [According to approved guidelinesand/or approved physician standing orders]
Zoledronic acid <i>Zometa</i>	As a single agent for treatment of tumor-induced hypercalcemia (TIH) [According to approved guidelines]	According to approved guidelinesand/or approved physician standing orders]







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